

HUMAN EMBRYOLOGY AND MORPHOLOGY

BY
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SIXTH EDITION
(REVISED AND ENLARGED)



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PREFACE

IN DECEMBER, 1901, I wrote a brief preface for the first edition of this book; now it is 1947 and, with the first preface before me, I am writing another for the sixth edition. I have to confess that, in the enlightenment which the intervening forty-six years have brought me, my original preface makes rather sorry reading. "Fifty years ago," my preface began, "it was possible for a teacher in a winter course of lectures to lay all the essential facts of embryology before his pupils; to-day fifty courses are not sufficient, so limitless have its subjects grown." In 1901, to be sure, the reconstructional method which Professor His of Leipzig had applied to human embryology during the last two decades of the 19th century with rare success was spreading abroad to all centres of anatomical research, so that the output of embryological fact was being multiplied, if not fifty times, at least many-fold. If such was the increase of 1901, what are we to say of the output of the present time? It is at least ten times that of 1901. Indeed, I suspect that many of my younger colleagues are of opinion that we knew nothing of real embryology at the beginning of the present century, meaning thereby that we knew only the dead anatomy of the embryo. Nothing of its living activities. Which, in a sense, is true, for living embryology is a growth of the 20th century. Perhaps a nemesis awaits my younger friends, for a century hence, at the present rate of progress, their successors will probably pass an equally hard verdict on their knowledge.

Having duly impressed my readers with the vast dimensions which the twin subjects embryology and morphology had attained at the beginning of the present century, I proceeded to explain how my choice of matter had been made. When the first edition appeared, I was teaching anatomy to students of the London Hospital. I thought then, and still think, that medical students do their work in the wards of the hospital all the better if they know something of the history of the human body. My book was based on demonstrations I gave to senior students during a winter session. "Each fact taught to the student," I wrote in 1901, "was necessarily one which was capable of application to his life's work, or by the possession of which he became a better workman. The extent to which each subject was dealt with was determined by its practical importance. In brief, clinical utility was the criterion applied." I would not defend that criterion now—the

criterion of utility. In subsequent editions my utilitarian ideal retreated more and more into the background. Who can tell what the clinical utility of any newly discovered fact may prove to be? Röntgen never dreamt that his discovery was to affect clinical practice in every corner of the world. I remember a time when we counted the facts relating to the behaviour of the nucleus during cell-division as idle knowledge, and now that same nucleus has become a microcosm wherein we see the machinery of heredity and of evolution at work. And so the basis on which embryological facts were admitted to my text broadened; everything which seemed to throw new light on our understanding of the human body was welcomed to my pages. Especially if such additions threw light on the history of the human body. Although I never forgot the needs of the medical student, the claims of the historian of the human body came to dominate my attention more and more.

One guiding principle has remained with me unchanged. I still maintain that Embryology becomes a profitable study only when we interpret its events in the light of evolution. We have to assume that multicellular forms of life were evolved from forms which were originally unicellular; that the vertebrate type arose from a larval stage of an invertebrate; that the vertebrate type was originally water-living and water-breathing; that air-breathers arose from a water-breathing ancestry; and that limbs arose from fins. The evolutionary principle as a source of guidance becomes particularly valuable when we seek to interpret the events which enable the embryo to become a parasite in the maternal womb. We have then to assume that viviparity was evolved from oviparity, and that the membranes in which the embryo and foetus become enclosed are but transformations of parts which at one time were included in the structure of the gut and body wall of a lower animal.

When the first edition of this book appeared, two lines of research were afoot which ultimately revolutionized our conception of vital processes, particularly those relating to growth and to development. In January, 1902, Bayliss and Starling announced the discovery of secretin, the herald of the hormone summer. I do not think Starling has ever received the recognition of his prescience. As evidence of this let me quote a passage from a lecture he gave in 1905 (*Lancet*, 1905 (2), 583): "If, as I am inclined to believe, all the organs of the body are regulated in their growth and activity by chemical mechanisms similar to those I have described, an extended knowledge of the hormones and their modes of action cannot fail to add largely to that complete comprehension of the body which is the goal of medical science." At the time Bayliss and Starling made their discovery, Hans Spemann in Germany

W. H. Lewis in America had each made independently an observation which seemed to have nothing to do with hormones, namely, the lens-forming power which the optic cup of the embryo exerts on the overlying ectoderm. The next important step forward in this second line of research was made by Spemann and Mangold when they demonstrated the power of induction possessed by the dorsal lip of the blastopore. The final discovery which linked those two separate lines of enquiry together and made them one came in the early 'thirties (Waddington, 1934), when it was found that the power of the dorsal lip of the blastopore to act as an "organizer" was due not to a living virtue resident within it, but to a dead chemical substance produced within it; in short, to a hormone. The story which I have been telling so imperfectly has been told in full by Dr. Joseph Needham in *Biochemistry and Morphogenesis* (1942). "Evocators," "inductors," hormones, as Dr. Needham rightly insists, can only call forth powers, capacities or competences which are already in existence within developing tissues; they are powerless to impart new properties or capacities to the tissues with which they come in contact. Thus the task which lies in front of embryologists is to discover the competences possessed by tissues and organs at each stage of their development and to isolate and identify the hormones which serve as evocators and organizers.

When the first edition of this book appeared, Germany was the centre of embryological and morphological research; that proud place has passed to the United States of America. The chief agent in effecting this transference was my gifted contemporary, Franklin P. Mall; it was he who laid the foundation of the school which has become our chief source of embryological fact—the Department of Embryology of the Carnegie Institution, Washington. His early death in 1917 seemed a loss that was irreparable, but under the direction of his successor and pupil, Dr. George L. Streeter, the Department of Embryology went from strength to strength; *Contributions to Embryology*, the publication of the Department, took its place in all the embryological laboratories of the world as the chief source of new knowledge, at least so far as the development of the human body was concerned. On Dr. Streeter's retirement in 1941, he in turn was succeeded by a pupil, Dr. George W. Corner. One can be certain that in Dr. Corner's hands there will be no falling away from the high standards established by his predecessors. My pages owe more to the American (Carnegie) School than to any other single source. One other important source I am glad to have this opportunity of acknowledging. It is the *Manual of Human Embryology*, by my friend—the late Prof. J. E. Frazer; I know of no text-book of embryology that is so packed with original observation as is his.

So much for past editions of this book. What of the present? Compared with the fifth edition, which appeared in 1933, the present (sixth) edition differs in the following ways :

The number of chapters has increased from XXX to XXXII. This is due to a division of two former chapters, XXVI and XXIX. Chapter XXVI was the second of two devoted to the urogenital system ; there are now three chapters devoted to this system, the new chapter, XXVII, dealing with the development and descent of the testicle, and the development of the adrenals. Chapter XXIX of the older edition was the second of two which gave an account of the development and evolution of the limbs ; there are now three chapters devoted to the limbs (XXIX, XXX, XXXI), the last being given to the processes of growth and of ossification as seen in the human skeleton, matters in which our knowledge has been expanding rapidly.

The number of figures has risen from 535 in the previous edition to 578 in the present. The new illustrations were drawn by Miss Mary Barclay-Smith. To her skill the author is greatly indebted.

The greatest change in the present edition will be seen in " Notes and References " given at the end of each chapter. These have been much expanded by references to recent papers which give original observations on matters dealt with in the text. In so loading these notes the author has had in mind the needs of teachers and of students who wish to take a hand in the good work of adding to what we now know of the development and growth of the human body. To these notes, also, have been transferred matters which are still subjects of debate or of doubt. On occasion, too, the author has used these notes as vehicles for the expression of personal opinion.

Hardly a page has escaped some degree of amendment ; in most chapters, several pages have had to be added. As these additions indicate the subjects which have received attention from embryologists since the issue of the last edition, it may be of interest to specify the more important. In Chapter I, there had to be incorporated accounts not only of very early stages of human development, but of the very earliest stages of primate development, based on specimens derived not from the human family, but from domesticated families of the rhesus monkey. In this way blanks in our knowledge of the earliest stages in the development of the human ovum have been filled in. To this new, reliable and accurate source of knowledge embryologists are indebted to the Carnegie Institution of Washington. Chapter II, which treats of placentation, had to be recast ; Chapter III, devoted to the origin of special embryonic structures, had also to be altered, new interpretative given and additions made, particularly relating to the mapping o .

"presumptive areas" on the embryonic shield. My chief difficulty with Chapter IV has been to keep it within bounds, for it is mainly concerned with that most fruitful and progressive of all branches of our subject, experimental embryology. For the greater part I have had to content myself by giving references to the leading works on this subject.

Many additions have been made to the four chapters (VIII, IX, X, XI) that are devoted to the development and morphology of the central nervous system. These relate to the development of nerve fibres, of the autonomic system, of the cerebellum, of the ganglionic masses of the fore- and mid-brain, and of the supragranular cortex. Especially important are the discoveries made in the rôle played by the neural crest; not only is it concerned with the formation of posterior root ganglia, the sympathetic system, the formation of nerve sheaths, but also with that of the pia-arachnoid and the development of face and pharynx.

In revising Chapters XII and XIII, which treat of the skull and face, I have obtained assistance from the writings of Prof. Brash, of Prof. H. A. Harris, of Prof. Wood-Jones, of Prof. De Beer and of Prof. P. D. F. Murray. Readers will find that in my pages the pre-maxilla has become again a bone of contention. In amending Chapter XVI (which deals with the eye and with vision), I received great help from Dr. Ida Mann's *Abnormalities of the Human Eye* (1937). Chapters XVIII and XIX, devoted to the pharynx and structures derived from it, required several additions, particularly concerning the origin and nature of paraganglionic bodies, wherein I have followed the lead of Prof. J. D. Boyd. It is unnecessary to specify alterations made to later chapters; they have been mentioned incidentally when giving my reasons for introducing two additional chapters.

To Prof. J. C. Brash, of the University of Edinburgh, and to Dr. A. J. E. Cave, of the Royal College of Surgeons of England, I owe a deep personal debt. They have brought to my notice errors and obscurities in the previous edition and made suggestions for the improvement of the present issue.

ARTHUR KEITH.

DOWNE, KENT.
July, 1947

I have taken the opportunity, given me by a reprint being called for of the present (sixth) edition, to amend certain details of my text and to make good some omissions. I am indebted to colleagues for drawing

my attention to these needed changes, especially to Prof. Cecil M. West, of Cardiff, to Prof. James Brash, of Edinburgh, and to Prof. A. N. Burkitt, of Sydney. Alas! it has not been possible to fall in with all their suggestions. Some of the defects to which they have called my attention lie in the history of this book; like its author it has grown old. The scientific terms used when the first edition appeared have been replaced by others; in some cases I have clung to the old names. Especially is this the case with illustrations that have done duty since the first edition appeared; they still bear the old but good names—*epiblast* for ectoderm, *mesoblast* for mesoderm, and *hypoblast* for endoderm. The blocks of these old illustrations have become worn and thin, but I am partial to them. Modern anatomists have banned the use of personal names in anatomical literature, which is a gain in many respects. But some of these names I am attached to—such as Rolando, Sylvius, Eustachius, Poupart, Hunter, etc.—and hence I have continued to use them. Some of my colleagues wish to have the older illustrations redrawn and the older nomenclature swept from my text. If at some future date a new edition were needed, these changes would merit consideration.—A. K.

CONTENTS

	PAGE
EARLY CHANGES IN THE DEVELOPMENT OF THE OVUM AND EMBRYO	1
THE MANNER IN WHICH A CONNECTION IS ESTABLISHED BETWEEN THE FOETUS AND UTERUS	31
THE PRIMITIVE STREAK, NOTOCHORD AND SOMITES . .	50
PHYSIOLOGICAL AND PATHOLOGICAL EMBRYOLOGY . .	63
AGE CHANGES IN THE EMBRYO AND FOETUS . . .	76
THE SPINAL COLUMN AND BACK	86
THE SEGMENTATION OF THE BODY	106
CENTRAL NERVOUS SYSTEM—DIFFERENTIATION OF THE BRAIN AND THE SPINAL CORD	117
THE MID- AND HIND-BRAINS	133
THE FORE-BRAIN OR PROSENCEPHALON	156
THE FORE-BRAIN OR PROSENCEPHALON (<i>continued</i>) . .	173
THE CRANIUM	205
DEVELOPMENT OF THE <u>FACE</u>	234
THE TEETH AND APPARATUS OF MASTIGATION . . .	266
THE NASAL CAVITIES AND OLFACTORY STRUCTURES . .	282
DEVELOPMENT OF THE STRUCTURES CONCERNED IN THE SENSE OF SIGHT	295
THE ORGAN OF HEARING	322
PHARYNX AND NECK	343
TONGUE, THYROID AND STRUCTURES DEVELOPED FROM THE WALLS OF THE PRIMITIVE PHARYNX . . .	364
ORGANS OF DIGESTION	379
ORGANS OF DIGESTION (<i>continued</i>)	406
CIRCULATORY SYSTEM	427

CHAP.	PAGE
XXIII ✓ CIRCULATORY SYSTEM (<i>continued</i>)	461
XXIV. RESPIRATORY SYSTEM	476
XXV UROGENITAL SYSTEM	500
XXVI ✓ UROGENITAL SYSTEM (<i>continued</i>)	529
XXVII ✓ UROGENITAL SYSTEM (<i>continued</i>)	551
XXVIII BODY WALL AND PELVIC FLOOR	565
XXIX DEVELOPMENT AND DIFFERENTIATION OF THE LIMB BUDS	592
XXX ✓ MORPHOLOGY OF THE LIMBS	611
XXXI ✓ DEVELOPMENT OF BONES AND JOINTS	633
XXXII ✓ SKIN AND ITS APPENDAGES	650
INDEX	667

HUMAN EMBRYOLOGY AND MORPHOLOGY

CHAPTER I

EARLY CHANGES IN THE DEVELOPMENT OF THE OVUM AND EMBRYO

The First Five Weeks of Development.—In the first 5 weeks of human development changes take place very rapidly. In that short time the fertilized ovum passes from the condition of a single cell, with a diameter of about $1/200$ of an inch or $125\mu^*$, to a fully formed human embryo about $1/5$ of an inch in length (5 mm.) and contained within a

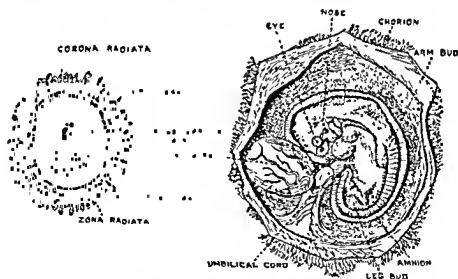


FIG. 1.

FIG. 1. The parts of a Mature Human Ovum. (Magnific. $\times 100$) (After Van der Stricht.)

FIG. 2.

FIG. 2. Human Embryo and its Membranes at the end of the 5th week of development (Magnific. $\times 3$.) (After Kollmann)

spherical envelope of embryonal membranes that measures nearly an inch in diameter (see Figs. 1 and 2). By the end of the 5th week the beginnings of all the parts of the adult body are recognizable—the head, the trunk, the limb-buds, the primitive segments, the eyes, the nose

* Measurements are given at first according to our English standard, but throughout this book the more convenient metric system will be employed. One inch = 25.4 mm. One millimetre = 1000μ , or micromillimetres, or microns.

growth of the pelvis, which becomes marked as the child learns to walk, and especially in the female at the time of puberty. The ovary, as is more frequently the case with the testicle, may be arrested in its descent.

In Fig. 4 an *earlier stage* is shown; it represents the condition about the beginning of the 3rd month. The ovary and tube with the remnants of the Wolffian body—a primitive form of kidney—occupy the position in which they are developed. Both are suspended by mesenteries from the dorsal wall of the peritoneal cavity, at the side of the mesentery of the gut.

Normal Position of the Adult Ovary.—When the ovary descends within the pelvis it usually occupies a definite triangle—the *ovarian*

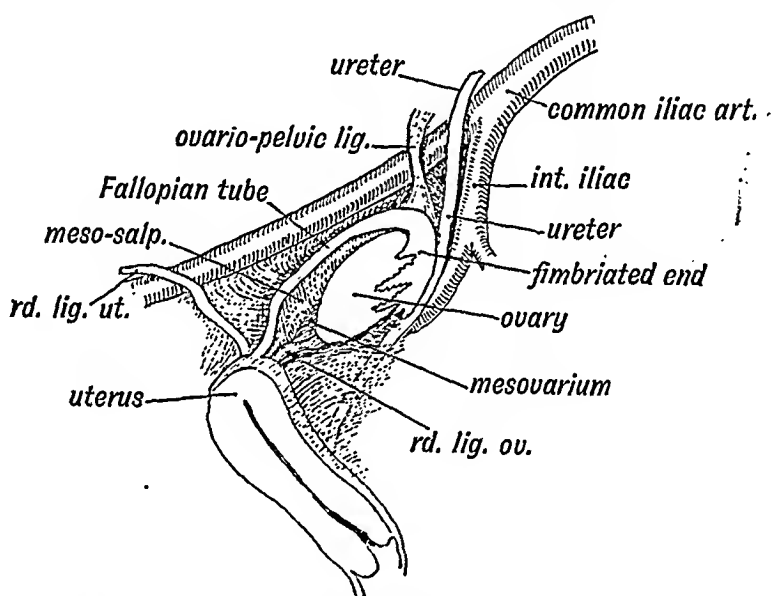


FIG. 5. Showing the position of the Ovary on the lateral wall of the Pelvis and its relation to the Fallopian Tube.

triangle—on the lateral wall of the pelvic cavity (Fig. 5). The ovarian triangle is bounded above by the upper or proximal half of the external iliac artery; below and behind by the internal iliac artery, with the ureter lying on the artery; in front by the reflection of the posterior layer of the broad ligament on the side of the pelvis. The peritoneum covering the triangle forms a depression, or occasionally a pouch, for the ovary. The fimbriated end of the Fallopian tube is normally applied to the ovary, ready to receive the ripe ova and transfer them to the uterus [2]. One of the fimbriae—the ovarian fimbria—tethers the tube to the ovary. It will be seen that, with the descent of the ovary, the mesosalpinx, the mesovarium and the common genital mesentery have come to form the major part of the broad ligament. The upper end of the common genital mesentery now forms the ovario pelvic ligaments (Figs. 3 and 5).

The ovary brings down with it, too, the ovarian arteries, veins, lymphatics and plexus of nerves. The nerves come through the aortic plexus from the 10th and 11th dorsal segments of the spinal cord, and the lymphatic vessels carry the ovarian lymph to a group of glands situated high up in the lumbar region.

An Ovum [3].—As the infantile ovaries descend, each is laden with thousands of ova; estimates vary from 70,000 to 100,000. The ova are embedded in the cortical stroma of the ovary, each being surrounded by a special company or cluster of epithelial cells, which provide both a nest and nourishment for the ovum or oocyte (Figs. 6 and 7). The cells that surround an ovum, with a condensed layer or theca of stroma cells outside them, form a *Graafian follicle*. The ovary is covered by a

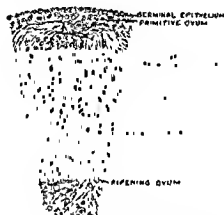


FIG. 6.

FIG. 6. Diagrammatic Section of the Ovary of a 5th-month Foetus, showing Nests of Germinal Epithelium and unripe Graafian Follicles.



FIG. 7.

FIG. 7. Ripe Graafian Follicle at Puberty.

cubical epithelium, derived from the *germinal epithelium* that formed a stratum on the free surface of the ovary at its first appearance in the roof of the abdominal cavity. The ova and their accompanying *follicular cells* are derived from the surface stratum. Amongst the columnar cells of the germinal epithelium and also in the stratum immediately beneath them are large peculiar cells. These are the *primordial ova* from which brood ova arise. The ova are thus carried within the ovary by ingrowths of the germinal epithelium. These tubular invasions into the ovary become broken up, the isolated masses of the germinal epithelium remaining to form the linings of the Graafian follicles. In the outer or cortical zone, follicles continue to form in early foetal life. It has been found that all the ova formed in early foetal life degenerate and disappear before the time of birth [4]. After birth, the formation of new ova continues; even up to the end of the fifth

directed backwards on the lateral pelvic wall above the ovary ; (c) the hand, infundibular or fimbriated part, folded backwards on the free border and exposed surface of the ovary. The tube is fastened by one of its fimbriae to the cranial pole of the ovary.

Course of the Ovum in the Tube.—The cilia on the fimbriae work towards the ostium abdominale, the abdominal mouth of the Fallopian tube, which is situated at the bases of the fimbriae, and carry the discharged ovum through the ostium within the tube. The ostium abdominale is shut when the tube is examined after excision ; the closure

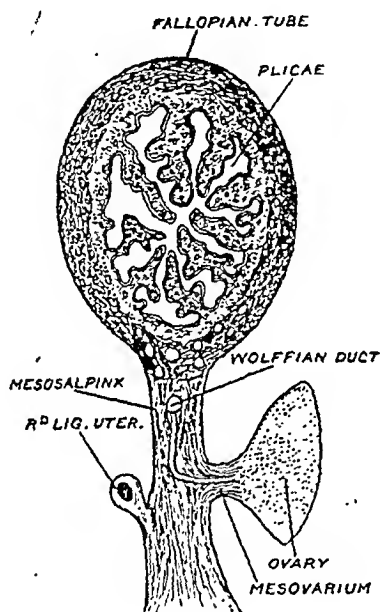


FIG. 8.

FIG. 8. Diagrammatic Section of the Broad Ligament and Fallopian Tube.

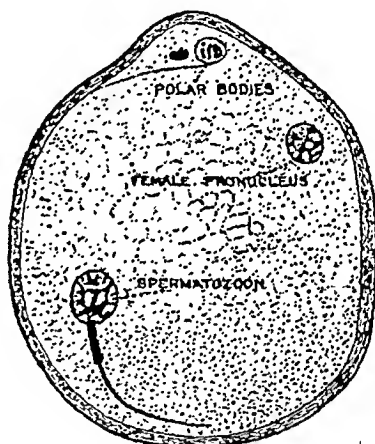


FIG. 9.

FIG. 9. Mature Ovum of Bat, showing the separate Polar Bodies, the Female Pronucleus and a Spermatozoon about to form a Male Pronucleus. (After Van der Stricht.)

is probably due to reflex contraction of the tube muscle, caused by handling and cutting. In the infundibular and ampullary segments of the tube, the mucous membrane is thrown into long plicated folds, shown in section in Fig. 8. They are covered with ciliated epithelium, which urge the ovum towards the uterus. Between these folds, in the upper reach of the tube, the ovum, if it is to be fertilized, usually meets the male cell or spermatozoon ; spermatozoa reach the sites of fertilization within a few hours of coitus, but lose their powers soon after their arrival in the tube [8]. The ovum, too, loses its powers a few hours after being shed. The passage of the fertilized ovum along the tube, assisted by peristaltic contractions, takes place slowly, for it undergoes its first developmental changes during this journey, which extends over a period

of 5 or 6 days. If the passage of the fertilized ovum is obstructed, which may result from an inflammation or cicatrization of the epithelial lining of the tube, development may proceed at the point of obstruction. When *tubal pregnancy* occurs, the growing ovum expands and ultimately perforates the tube—usually in the 2nd month—an accident which is always attended by a grave haemorrhage.

The History of the Ovum within the Fallopian Tube.—When the ovum enters the Fallopian tube, it is a cell of very considerable size (120 to 150 μ), with a cell wall (the *zona pellucida* or *radiata* (Fig. 1)), a nucleus (the *germinal vesicle*) and a nucleolus (the *germinal spot*). The ovum prepares for fertilization by the extrusion from its nucleus of first one, then a second *polar body*, and, with the extrusion, the germinal vesicle becomes the *female pronucleus* (Fig. 9). The first polar body is shed as the ovum ripens in its Graafian follicle; the second separates in the tube after the sperm enters the ovum [9]. The polar bodies or polocytes, for they really represent cells, lie outside the protoplasm of the ovum, but within the *zona pellucida*; they are parts of the germinal vesicle, which are extruded with all the display of karyokinesis—the peculiar changes manifested by the nucleus when a cell is about to divide. We shall see that the three polar bodies really represent three aborted ova—which have left their cell bodies behind them to enrich that of the principal ovum.

Karyokinesis.—The preparatory or maturation changes that take place in the nucleus of the ovum and also in the nucleus of the male germinal cell are of the greatest interest to us, for we have good grounds for suspecting that the mechanism that regulates the shaping of the adult body is represented in the substance of the nucleus of the germ cell. The nucleus appears to be the chief vehicle of heredity—the medium by which the features of parents are handed on to the child. Hence the importance attached by embryologists to the elaborate changes undergone by the nucleus of a maturing male or female germ-cell. When an ordinary cell of the body is about to divide, the nucleus undergoes certain changes before cleavage takes place. The nuclear division precedes that of the whole cell. This mode of cell division or cell propagation is known as karyokinesis or mitosis. Two elements within the nucleus play a part in the process—the *chromatin*, which readily combines with certain staining reagents, and the *achromatin*, which does not absorb dyes. In the resting phase, the chromatin is scattered as minute particles in the substance of the nucleus, but when mitosis is to take place the particles unite into filaments; these filaments break up into segments or rods, each rod being known as a *chromosome* (Fig. 10). The chromosome number for man is 48; they are arranged

Formation of Spermatozoa.—Having thus described the maturation of the ovum, and followed it within the Fallopian tube, it is necessary to trace the history of its counterpart in the male—the spermatozoon [11]. The manner in which a spermatozoon is produced by a primary and secondary division from a *spermatocyte* is very similar to the production of a *mature* from an *immature* ovum. The form of mitosis is the same (heterotypical), the chromosomes being reduced to 24 in number and to a peculiar shape. The two divisions take place within the seminiferous tubules of the testis, and result in the production of four spermatozoa, corresponding to the mature ovum and three polar bodies (Fig. 11, *B*). It is in the first of these two divisions that reduction takes place. The seminiferous tubules correspond to the earliest in-

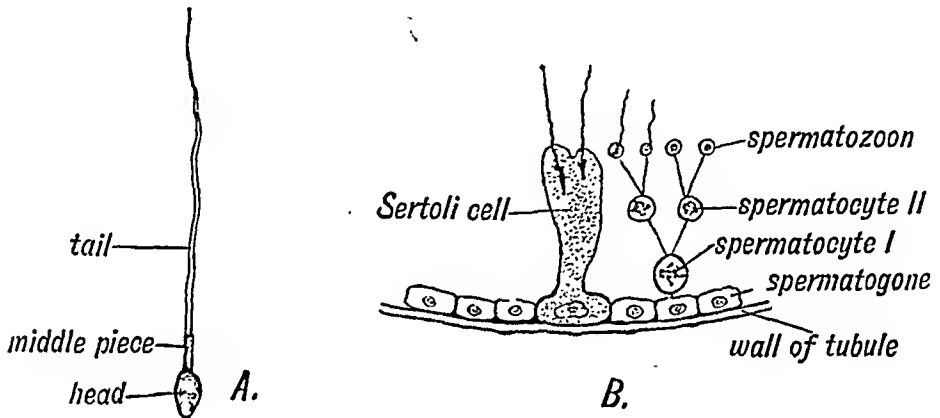


FIG. 11.

A. Diagram of a Spermatozoon.

B. Diagram showing the origin of Spermatozoa from the lining cells (spermatogonia) of the tubules of the testicle.

growths of germinal epithelium that carry the primordial ova within the medulla of the ovary. Lining the tubules are two kinds of cells: those of Sertoli (Fig. 11, *B*), large cells for nourishing the spermatozoa, representing those of the stratum granulosum in the Graafian follicles; and other cells known as spermatogonia, corresponding to primordial ova. Spermatogonia divide and give rise to primary spermatocytes, which correspond to immature ova. A primary spermatocyte divides into two secondary spermatocytes, each of which again divides, and thus four cells are produced, which become modified into spermatozoa (Fig. 11, *B*). The nucleus forms the head, the junctional part represents the centrosome, while the tail is all that remains of the substance of the cell body (Fig. 11, *A*). The ripe ovum has a diameter of about 130μ , whereas the total length of a spermatozoon is only 50μ . While the ovum represents a large passive cell, laden with nourishment or yolk, its male counterpart becomes highly modified within the Sertol

or nurse cell, has its cell substance reduced to a minimum and develops a power of active motion. Ova ripen singly; spermatozoa, on the other hand, ripen by the million. Spermatozoa can be kept alive for many days in nutritive media [12]; probably the secretions of the epididymis, vesiculæ seminales, prostate and Cowper's glands are for this purpose.

Fertilization.—In the course of fecundation many millions of spermatozoa are lodged in the genital passage; some stem the adverse current of the uterine cilia, and so reach the interlaminar grooves in the wider parts of the tube. In the course of its descent within one of the grooves the egg may be fertilized. The spermatozoon, attracted to the ovum by a force we do not yet understand, bursts through the zona pellucida, loses its tail, its head enlarges, and forms the *male pronucleus*. The male and female pronuclei unite, and from their union springs the nucleus of the fertilized ovum. This is the centre from which all futuro developmental changes start. In the pronuclei, it will be remembered that the chromosomes were reduced to half the usual number; by their union the full complement of 48 is again restored in the fertilized ovum. By the process of fertilization, the characters of two human individuals are mingled. The ovum may be, but rarely is, fertilized in the ovary, or between the ovary and ostium abdominale, the result being a pelvic gestation. The fertilized ovum reaches the cavity of the uterus about the 6th day and prepares for implantation. During its passage it undergoes repeated segmentations. The musculature of the tube, as well as the action of the cilia, assists the fertilized and developing ovum in its progress towards the cavity of the uterus.

Formation of the Embryo.—We are now to follow, step upon step, the changes which are to transform the fertilized ovum into a human embryo. With the fusion of the male with the female pronucleus the ovum begins to divide, thus giving rise to the first brood of cells, two in number [13]; these in turn give rise to a second brood, four in number, and so on through successive stages, until a minute mass of cells replaces the ovum (Figs. 12 and 13) and thus a *blastula* or *morula* is formed—the first stage in the production of an embryo.

The production of the blastula takes place as the egg passes towards the cavity of the uterus, but before it has come into actual contact with the prepared lining membrane or decidua, it has entered a second and very important stage. A space or cavity appears within the blastula (Fig. 14) so that its cells become arranged in a definite manner. The cells which are going to give rise to the structures by which the embryo is to be nourished become arranged around the central cavity as a covering layer, while the cells which are to build up the embryo and its enveloping membrane, known as the amnion, are enclosed within the

group having a separate developmental destiny. First, there are those (95 in number) just under the enclosing layer of trophoblast that go to the formation of the enclosing membrane, the *amnion*, and may be named amniogenic or amnioblastic. The cells of the inner mass that are to give rise to the embryo may be called embryogenic or, collectively, the embryoblast; they are only 32 in number. Finally, there is the primitive or blastocystic endoderm; it forms the deepest and thinnest stratum of the inner cell mass; in Fig. 15 it is seen to be spreading beyond the limits of the inner cell mass, and will ultimately enclose the cavity of the blastocyst.

How actively development is proceeding at this stage may be seen from Fig. 16, which represents the state reached on the 10th day. The trophoblast over the inner cell mass had invaded the hypertrophied mucous membrane of the uterus (endometrium) and is actively proliferating, absorbing the invaded tissues, thus obtaining a means of sustenance. Changes are taking place in the inner cell mass; in its amniogenic cells a cavity has appeared, the cavity of the amnion. The endodermal stratum is now more distinct and is seen to be spreading outwards on the wall of the blastocyst. Implantation is not complete; the area of the trophoblast wall, opposite to the inner cell mass, is still exposed and will gain an attachment to the opposite wall of the uterine cavity. But in man, and in anthropoid apes, the whole of the blastocyst becomes embedded; implantation is complete in them. In them too, the point at which entry is made is sealed up by a fibrinous cap.

In the 12th day the developing blastocyst of the macaque enters another stage. The three constituents of the inner cell mass—embryonic, amniogenic and primitive endoderm—have set out to build embryo, amnion and primitive yolk-sac. The amniotic cavity has expanded; in its floor the embryonic cells now form a double layer or plate, an upper or ectodermic and a lower or endodermic. In the development of all vertebrates the yolk-sac is developed in two parts. There is first the part that contains the yolk; this is the part represented by the cavity of the blastocyst of the macaque—the blastocele. The second part is developed later, between the embryo and the stock of yolk; it is this later part of the yolk-sac which appears in the macaque blastocyst on the 12th day; it constitutes the true or permanent yolk-sac. Thanks to Drs. Streeter and Heuser we now know that the yolk-sac of the human embryo has the same two stages in its development.

Such, then, are the stages which the blastocyst of the macaque passes through in the earlier days of the 2nd week of development. We turn now to the corresponding stages of the human blastocyst [14]. Although these stages have now been found (p. 29) it will be profitabl

to look for a moment at the hypothetical reconstructions we had made of them. Such a reconstruction is depicted in Fig. 17. The blastocyst is shown completely embedded in the endometrium; it is now known that the human blastocyst is implanted precociously—by the 8th day. The blastocyst wall is not thick, as shown in the diagram, but is made up for the greater part of a single layer of cells; only in the deeper parts is the trophoblast proliferating rapidly and spreading into the endometrium. Two cavities are shown: the amniotic enclosed by ectoderm; the vitelline cavity enclosed by endoderm. The bilaminar embryonic plate separates the two cavities. The cavity of the blastocyst—the blastocele—is depicted as filled by a fine reticulum, which is the first

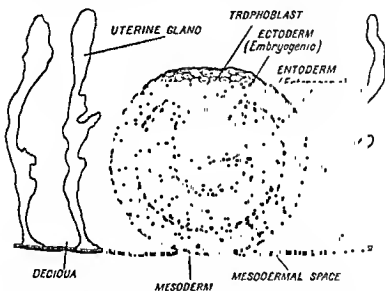


FIG. 17. A hypothetical reconstruction of a Human Blastocyst at a stage reached early in the 2nd week of development

of the mesoderm to be developed. The mesoderm in Fig. 17 has been given too precocious and too dense a representation. The yolk sac has not the definite wall shown in that figure; only the roof, the part underlying the embryonic plate, has a definite existence; the rest of the cavity represented as bounded by endoderm is hard to distinguish from the reticular mesoderm. All the mesodermal tissues lying between the cavity of the endoderm and the trophoblastic wall are derived by delamination from the layer of ectoderm which constitutes the trophoblastic wall.

In Fig. 18 is represented another hypothetical stage—that reached by the human blastocyst at the end of the 2nd week. In Fig. 17 a space or cleft is shown in the fine reticular mesodermal tissue; in Fig. 18 this cleft has extended throughout the blastocyst, separating amnion and

archenteron (yolk sac) from the enclosing wall of trophoblast by a wide space—the extra-embryonic coelom. The trophoblastic wall has now a lining of mesoderm, while the walls of the amnion and archenteron receive a similar covering. Now, if the yolk sac cavity shown in Fig. 17 had become the yolk sac of the stage represented in Fig. 18, as we all assumed it did, then the account just given could not have turned out to be erroneous. It is now known that the yolk sac and its surrounding reticular tissue (shown in Fig. 17) are pressed back and disappear when the coelomic cavity is formed, while a new or permanent yolk sac

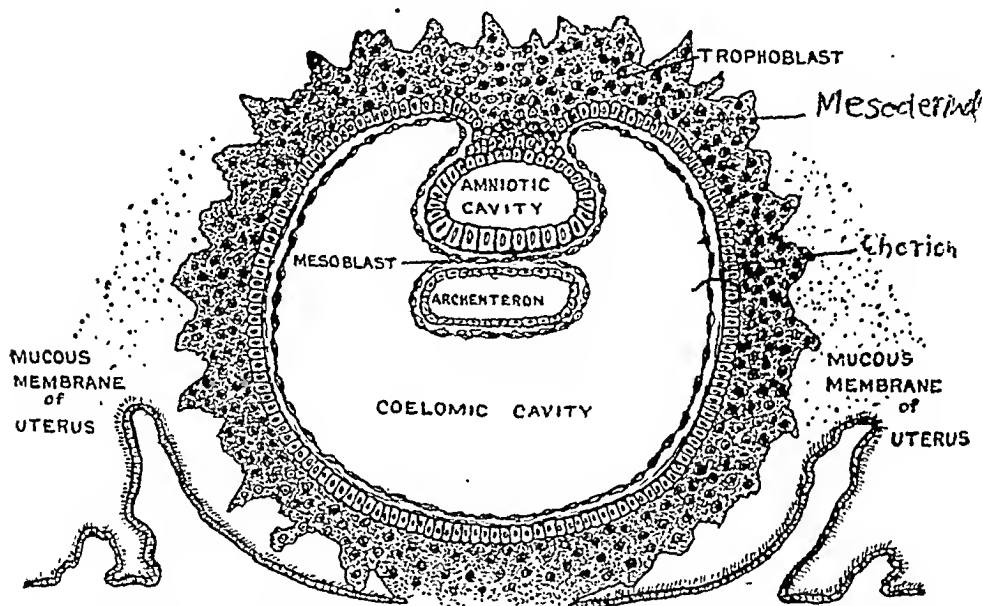


FIG. 18. Hypothetical reconstruction of the stage reached by a Human Blastocyst at the end of the 2nd week of development. The mesoblast (mesoderm) of the Blastocyst was at one time believed to arise from the Embryonic Plate. (After T. H. Bryce.)

is formed from the roof of the old one. It is the permanent yolk sac that is depicted in Fig. 18.

When we enter on the stages passed through by the human embryo in the 3rd week of development we leave hypothesis behind us; there are so many observations to guide us. In 1899 Dr. Peters gave a full and clear description of the stage reached at the beginning of the 3rd week [15]. The whole blastocyst was as yet of small size—only 1.6 mm. (1/16 in.) in its longest diameter (Fig. 19). The enveloping trophoblast, which is ectodermal in nature, with its lining of mesoderm, now receives the name of *chorion*, although, as yet, it is non-vascular. It draws sustenance from the endometrium. The archenteric vesicle (yolk sac) is still of minute dimensions (Fig. 19). The amniotic cavity formed within the enclosed ectoderm is larger, and the cells lining it have

become differentiated into two kinds (Fig. 19). An area of columnar cells, forming the floor plate of the cavity, produces ultimately the epithelial covering of the body, and all the cells and fibres of the nervous system. The flatter cells that line the dome of the cavity will form the epithelial lining of the Amnion; the outer layer of mesoderm affords a covering to the amniotic ectoderm (Fig. 19). Fluid collects within the cavity of the amnion; floating in the fluid, the human embryo will develop. Thus the delicate embryonic tissues, being equally supported

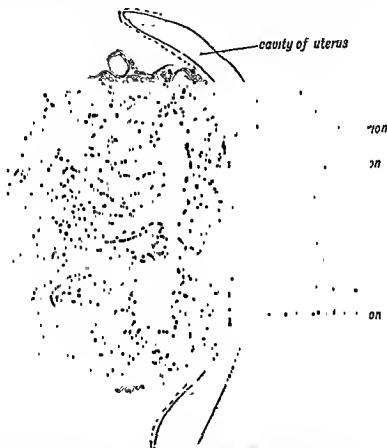


FIG. 19 The stage of development reached by the Human Blastocyst at the beginning of the 3rd week of development. It is embedded in the lining membrane of the Uterus (Modified by F. Wood Jones from drawings given by Peters and Selenka)

on all sides by the amniotic fluid, may pursue their developmental courses, unhindered by the influence of gravity and uninjured by the pressure to which the uterus within the abdomen is subjected by the movements of respiration or bending of the trunk. If the fluid is deficient or absent, then many forms of malformation may result.

At the stage represented in Fig. 19 it becomes possible to detect the foundation or *Anlage* of the embryo. It is represented by the bilaminar plate of tissues that separates the cavity of the archenteron from the cavity of the amnion. The growth of the embryo remains in abeyance;

all the developmental energy is thrown into the upbuilding and expansion of the enveloping ectoderm or *trophoblast*, as Hubrecht named it in 1889, for he recognized that its chief function was to provide the embryo with the means of nourishment (*τροφός*, a feeder). Thus in the earlier stages of development, while the embryonic rudiment remains in abeyance, the tissues that protect and nourish it grow and develop with exceeding rapidity. Indeed, although the stage shown in Fig. 19 is that reached about the 15th day, the embryo is still very little larger than the original ovum. On the other hand the epithelium forming the trophoblast has become differentiated into: (a) a *Basal Layer* (Langhans' cells); (b) masses of cells, which have undergone multiplication without separation; this formation is known as *syncytium* (Fig. 19). The syncytium is chiefly formed on that aspect of the developing ovum which is directly in contact with the wall of the uterus. It is remarkable not only for the imperfect separation of its cells, due probably to the rapidity of its growth, but also for the extraordinary power it exercises on the mucous membrane of the uterus. Processes of the syncytium burrow within the thickened and vascular mucous membrane in a systematic and regulated manner; they absorb the tissue with which they come in contact, and lay open blood-vessels of the mucous membrane. The maternal blood escapes into spaces enclosed by the syncytial processes or into lacunae formed by the vacuolation of processes. No true villi are formed as yet. In certain circumstances syncytial cells escape into the general circulation and form malignant growths. If the developing ovum be arrested in the Fallopian tube the syncytium, owing to the extreme thinness of the lining membrane, quickly eats its way into and through the wall of the tube.

In Fig. 21 there is given, in a diagrammatic form, the stage of development reached about the end of the 3rd week. A very rapid growth sets in during this week; the chorionic vesicle, which at the stage just described (Fig. 19) measured only 2 mm. in its longest diameter, has become five times that size—an object easily visible to the naked eye. Villi begin to grow out, at first simple finger-like processes of trophoblast; they project into spaces or lacunae filled by maternal blood. The trophoblastic core of the processes becomes converted into angioblastic (mesodermal) tissue. Thus the chorion, besides its original lining of mesoderm, obtains an additional supply by a direct transformation of trophoblast (ectodermal in nature) into mesoderm. Towards the end of the 3rd week villi begin to branch. Blood-vessels and blood begin to form within the branched villi towards the end of the 3rd week, but a circulation from the heart is not initiated until early in the 4th week.

Thus, for the first three weeks the human embryo depends on the endometrium for its supply of nutriment.}

By the end of the 3rd week the embryo is definitely represented by a plate or shield—the *embryonic plate* (Fig. 20)—composed of three layers of cells—an upper or ectodermal, forming a floor to the amniotic

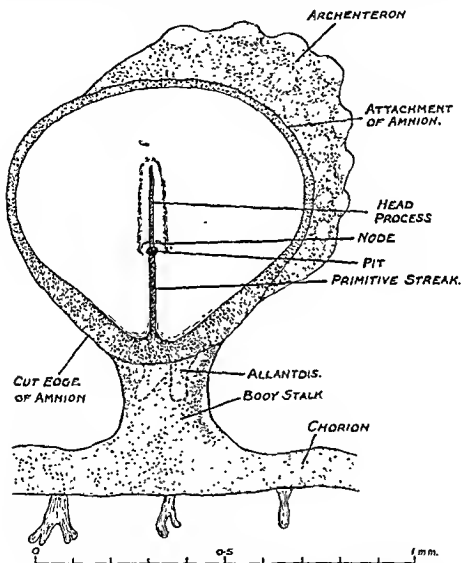


FIG 20. A Human Embryonic Plate at the end of the 3rd week of development. It is viewed from above after the amnion has been removed. The length of this Embryonic Plate was 0.9 mm. (Thompson and Brash)

vesicle; a lower or endodermal, serving as a roof for the endodermic vesicle, and an intermediate layer of mesoderm (mesoblast) now in process of development. On the upper surface of the flat embryonic plate, which at the end of the 3rd week has a total length of 1.5 mm., appears, in its hinder or caudal half, the *primitive streak* (Fig. 20). At the anterior end of the streak an important centre of growth and of

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The allantois should be regarded as an outgrowth from the *primitive* yolk sac. The embryonic plate, with the amniotic and archenteric vesicles, is bound to the chorion by the *body stalk* (Figs. 20, 21 and 22)—the rudiment of the umbilical cord. Thus towards the close of the 3rd week a human pregnancy is represented by (i) an embryonic plate, (ii) a yolk sac and allantois, (iii) amnion, (iv) body stalk, (v) chorion.

We shall now concentrate our attention on the growth of the embryo, which from the end of the 3rd week to the end of the 5th undergoes a very rapid transformation [17]. The changes to be described follow

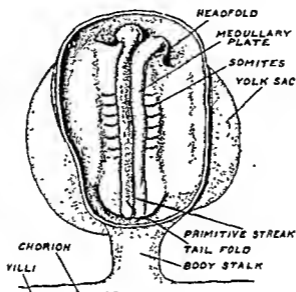


FIG. 22. The formation of the Medullary Folds and Somites on the embryonic plate.
(From Prof. Pfannenstiel's model of an embryo measuring 1.95 mm. in length.)

very rapidly. At the beginning of the 4th week two folds—the *medullary folds*—begin to rise up along the head end of the embryonic plate (Fig. 22), thus demarcating the neural plates from which the brain and spinal cord are to be developed. The rising up of the medullary folds is accompanied by the appearance of another very important developmental process—the cleavage or *segmentation* of the mesoderm on each side of the medullary folds into segments or somites. Segmentation begins in what will become the occipital region of the head and spreads rapidly backwards, some 24 or 26 somites being separated before the end of the 4th week. Thus the hinder head region of the embryo is the first to be differentiated and we have every reason to suppose that the segments at the cranial end are the oldest in an evolutionary sense.

organization is coming into being [16]. The ectoderm at the anterior end of the streak grows rapidly and rises up into an elevation or node named the *primitive node*, the representative of the dorsal lip of the blastopore.

The funnel-shaped pit at the cephalic end of the streak represents the anterior part of the blastopore; the primitive (Hensen's) node, its anterior or dorsal lip. A process from the node grows inward and forward on the roof of the archenteron. This ingrowth of ectoderm is known as the *Head Process* and plays a most important part in the development of the embryo [16]. The process becomes hollowed; its floor opens, and thus a communication is established between the cavities

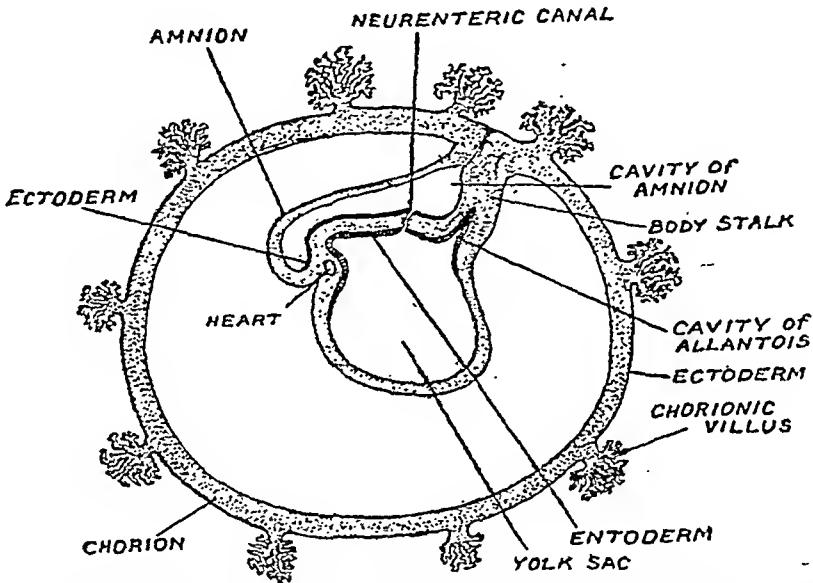


FIG. 21. Diagrammatic Section of a Human Pregnancy towards the end of the 3rd week of development, showing its demarcation into embryo and membranes. (After Graf Spee.)

of the amnion and archenteron. This communication is known as the *neurenteric canal* (Fig. 21). The nature of the primitive streak and of the neurenteric canal we shall discuss later (see p. 50). The archenteric vesicle by the end of the 3rd week has also undergone a rapid growth, now measuring 2 mm. in diameter, and we can recognize in it (see Fig. 21) the beginning of a division into two parts: the definitive, as contrasted with the earlier or primitive, *yolk sac*—which will come to lie outside the embryo; and a part which remains applied to the embryonic plate and will form the alimentary canal system. The part which will come to lie within the embryo already shows a division into three parts: a forward diverticulum—the rudiment of the *foregut*; a posterior diverticulum—the rudiment of the *hind gut*; and an outgrowth of the hind gut—which represents the structure known as the *allantois* (Figs. 20 and 21).

cells along the median dorsal wall of the archenteron is separated as a tube to form the *notochord* (Fig. 24, *A* and *B*). This chordal strip, although continuous with the archenteron is derived, as we shall see, from the ingrowing process at the anterior end of the primitive streak. Round the notochord are developed the spinal column and the greater part of the base of the skull. (iii) Indications are to be seen of a separation of the archenteron into an intra-embryonic part, which will form the *alimentary tract*, and an extra-embryonic part, which becomes the *yolk sac*. (iv) The embryonic mesoderm, which, as we shall see in Chapter III, arises as an ingrowth from the primitive streak, lies on each side of the

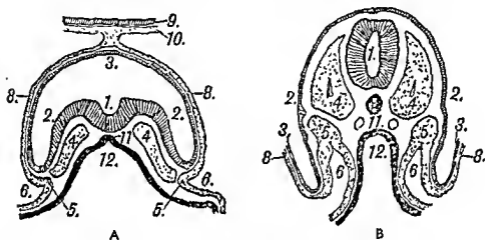


FIG. 24. Schematic Transverse Sections of two Human Embryos.

A, Late in the 3rd week of development. *B* Late in the 4th week of development. The numbers are placed on corresponding points: Ectoderm, shaded; endoderm, black; mesoderm, stippled

- 1. Somatopleure
- 2. Somatopleure
- 3. Somatopleure
- 4. Paraxial mesoderm.
- 5. Intermediate cell mass.
- 6. Coelom, bounded by the somatopleure externally and splanchnopleure internally
- 8. Mesoderm on amnion.
- 9, 10. Chorion
- 11. Notochord
- 12. Archenteron

notochord, and becomes divided into the following parts: (a) *paraxial mesoderm* (4, Fig. 24), from which the voluntary musculature, as well as other parts of the body system, arises; (b) *intermediate cell mass* (5), in which the renal and genital organs are developed; (c) *somatic mesoderm*, this layer with the *ectoderm* over it forms the *somatopleure*, the outer wall of the coelom; from the coelom are developed the pericardium, pleura and peritoneum; (d) the *splanchnic mesoderm*, which covers the intestine and yolk sac; the *splanchnic mesoderm* and *endoderm* together form the *splanchnopleure*. (v) Indications can be seen of the division of the coelom into intra- and extra-embryonic parts (6, Fig. 24). When the umbilicus contracts and closes, these two parts of the coelom are finally separated. It is also during the 4th week that

With the appearance of somites the human embryo manifests its vertebrate character.

The human embryo shown in Fig. 23 exemplifies the great advance made during the 4th week. The medullary folds have fused along their crests and enclosed the neural plates to form a canal or tube; the process of segmentation is spreading rapidly backwards; the head and gill arches can now be recognized, and although the embryo measures as yet less than 3 mm. in length, the main parts of the adult body, saving the limbs, are clearly foreshadowed.

We have reached the state of development exhibited by a human

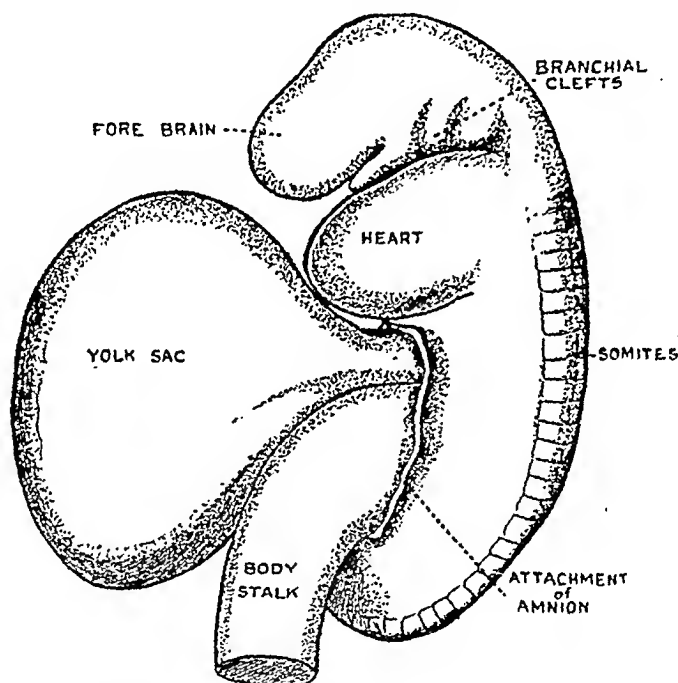


FIG. 23. Human Embryo 2.5 mm. long, towards the end of the 4th week of development. (Professor Peter Thompson.)

embryo at the end of the 4th week. We must now turn to some of the chief internal changes that have been taking place, and this can best be done by comparing a section across the flat embryonic plate of a pregnancy in the 3rd week of development with one from an embryo in the 4th week. When such sections (Figs. 24, *A* and *B*) are compared the following changes will be noted: (i) A narrow plate of modified ectoderm or epiblast, stretching along what will be the median dorsal line of the body, becomes depressed, thus forming the floor of a groove; the lateral margins of the groove rise up, meet together and fuse along the middle line. Out of the *neural tube* thus enclosed are developed the brain and spinal cord. (ii) In a somewhat similar manner a strip of

when the wall of the yolk sac became differentiated. When the coelomic cavity is developed they migrate towards the genital ridges. There is nothing strange in such a migration, for it is a daily occurrence in the adult body for leucocytes to be drawn in crowds to a site of infection under an obscure attraction that is named *chemiotactic*. Although it is now generally agreed that primordial ova do arise in the early embryo as just described, it is also certain that ova continue to arise from the epithelium covering the ovary from birth onwards, but particularly at the period of puberty [18]. After the complete eradication of the testes of birds, new and fertile organs may be produced from the dorsal tissues of the abdomen. It was at one time believed that teratomata, tumours

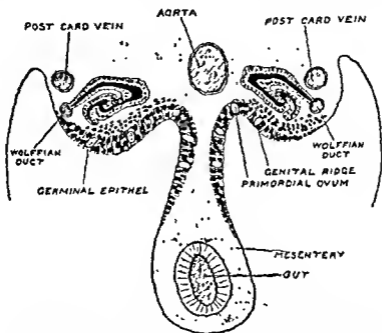


FIG. 26. Diagrammatic Section of the roof of the Coelomic cavity of a Human Embryo in the 5th week of development, showing the position of the Genital Ridges in which the Ovary or Testicle is formed.

made up of aberrant embryological tissues, might arise from primordial ova that had gone astray. This theory is now discarded.

Determination of Sex.—Amongst the chromosomes of the nucleus there is a pair that is believed to be directly connected with the determination of sex. In the female nucleus they are known as the *x-x* pair; in the male, as the *x-y* pair. At their reduction spermatozoa may retain either the *x* or the *y* member of the pair. Half of them retain the *x* chromosome and may be called "female-producers"—for when the male pronucleus adds its *x* to the *x* of the pronucleus of the ovum, the *x-x* or female pair will result. Half of the spermatozoa retain the *y* chromosome and are "male-producers"; when united with the ovum,

the paraxial mesoderm becomes separated into primitive segments, or *somites*, formerly known as protovertebrae. In the embryo shown in Fig. 23, 23 pairs are already separated.

In Fig. 25 is represented the fully differentiated human embryo—a stage of development reached about the end of the 5th week. From crown to rump the embryo about this time measures 5 mm. ($\frac{1}{5}$ of an inch). The buds of the upper and lower extremities have now appeared; segmentation has reached almost to the tip of the tail, there being 3 occipital and 35 body somites, the last representing the 6th coccygeal or caudal. The mouth is becoming apparent; so are the eyes and nose; the gill arches, four of which are apparent in the neck, have

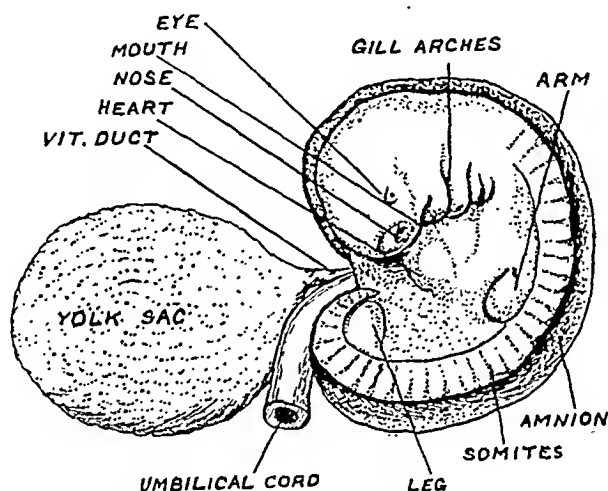


FIG. 25. Showing a Human Embryo, 5 mm. in length, at the end of the 5th week of development. (After Keibel and Mall.)

reached their highest development; a blood circulation is now fully established, the body stalk having been transformed into the umbilical cord. The yolk sac is now joined to the embryonic gut by a long narrow duct—the vitello-intestinal duct (Fig. 25).

Origin of Ova and Spermatozoa.—Towards the end of the stage just described, the *genital ridges* arise from the intermediate cell mass and project into the coelom, one at each side of the root of the mesentery (Fig. 26). The mesothelial cells that line the coelom assume a columnar form at the root of the mesentery and over the genital ridges; between these cells appear *primitive germ-cells* (primordial ova), characterized by their large size and reaction to certain stains. Hitherto it has been assumed that the germ cells arose from the mesothelial columnar cells that cover the ridge. Beard, during a prolonged and accurate investigation of the development of fishes, especially of the skate, discovered that the germinal cells were not formed in the genital ridges but appeared

Contrib. Emb., 1942, 30, 87. The observations that led to the discovery of the secretions or hormones formed in the corpora lutea have been summarized by Dr. Corner in the *Trans. Obstet. Soc. Edin.*, 1937, p. 61.

[7] For a statement of our knowledge of the functional relationships between pituitary and ovary, see Hartman, C. G., *Contrib. Emb.*, 1942, 30, 113; Thompson and Cushing, *Proc. Roy. Soc.*, 1934, 115 (B), 88; Marshall, F. H. A., *ibid.*, 1937, 122 (B), 413; Harris, C. B., *ibid.*, 1937, 122 (B), 374; Clark, W. E., Le Gros and others, *Jour. Anat.*, 1938, 73, 152; *Sex and Internal Secretion*, edited by Allen, E., 1932; Pfeiffer, C. A., *Amer. Jour. Anat.*, 1936, 58, 195; Billiter, Q. A., *ibid.*, 1936, 60, 357; Saxton and Loeb, *Anat. Rec.*, 1937, 69, 261; Gatz, A. J., *ibid.*, 1938, 70, 619; Clarke, Albert and Selye, *ibid.*, 1943, 83, 449. For chemistry of gonadotrophic hormones, see Freund, J., *Nature*, 1938, 141, 1014; Needham, J., *Biochemistry and Morphogenesis*, 1942, p. 176.

[8] For movements of spermatozoa and their survival in uterus, see Mann, T., *Nature*, 1945, 156, 80; Phillips and Andrews, *Anat. Rec.*, 1937, 78, 127; Parkes, G. H., *Phil. Trans.*, 1931, 219 (B), 381.

[9] It is now agreed that in mammals the first polar body is separated before the ovum is shed from its follicle, and that the second polar body is separated while the ovum is in the tube and about to be fertilized. See Hamilton, W. J., *Jour. Anat.*, 1944, 78, 1; Flynn, T. T., and Hill, J. P., *Trans. Zool. Soc. Lond.*, 1939, 24, 446 (ova of Monotremes). For size of pronuclei, see Mainland, D., *Jour. Anat.*, 1930, 64, 262; Hamilton, W. J., *ibid.*, 1936, 70, 429.

[10] For recent literature on chromosomes see Darlington, C. D., *The Evolution of the Genetic System*, 1939; *Nature*, 1942, 149, 66 (on chemistry of chromosomes); Waddington, C. H., *An Introduction to Modern Genetics*, 1939; *Organisers and Genes*, 1940; Goldschmidt, R., *Physiological Genetics*, 1938; Haldane, J. B. S., *Nature*, 1936, 137, 398; Koller, P. C., *Proc. Roy. Soc. Edin.*, 1937, 47, 194 (for sex chromosomes); de Winiwarter, H., *Archiv. Biol.*, 1938, 49, 111; Cowdry, E. V., *Text Book of Histology*, 1935; Roberts, J. A. Frazer, *An Introduction to Medical Genetics*, 1940.

[11] For structure and formation of spermatozoa, see *Human Embryology*, by Hamilton, Boyd and Mossman, 1945, p. 7; Froriep, E., *Anat. Anz.*, 1936, 82, 1.

[12] Spermatozoa are anaerobic if kept in a medium containing glucose; see Mann, T., *Nature*, 1945, 156, 80.

[13] For an account of the cleavage of the macaque ovum, see Lewis and Hartman, *Contrib. Emb.*, 1933, 24, 187; Wislocki and Streeter, *ibid.*, 1938, 27, 1 (changes after the 8th day); researches into the embryology of the rhesus monkey, made by

segmentation of the rabbit ovum has been described by G. G. Pincus, *Proc. Roy. Soc.*, 1930, 107, 132; for respiratory exchange during segmentation, see *Biochemistry and Morphogenesis*, by J. Needham, 1942.

My account of the development of the blastocyst of the rhesus monkey is based on the researches of Heuser and Streeter, published in *Contributions to Embryology*, 1941, 29, 15.

[14] Dr. Streeter announced the discovery of these two early embryos in the *Year Book of the Carnegie Institution*, Washington, 1939, p. 147. With these two embryos the Institution acquired the blastocyst of a chimpanzee in the 11th day of development, the earliest stage of anthropoid development known. Like the human blastocyst, and unlike that of the monkey, the blastocyst of the chimpanzee becomes completely embedded in the endometrium. An account of

the x - y or male pair is produced. The determination of sex by chromosomes is not absolute; as we shall see (p. 67), the sex of an individual may be reversed in the course of development; occasionally both sex elements may co-exist in the same individual.

Thus in the space of 5 weeks the cycle that produces new human seed from the old is accomplished and all the parts of a new human body are laid down in outline. In these 5 weeks the fertilized ovum has given rise to (i) germ cells that are endowed with the combined properties of the ovum and spermatozoon from which they were produced; (ii) an embryo in which these cells are nourished and protected; (iii) membranes by which the embryo is protected and nourished during intra-uterine life.

Having thus followed the chief developmental changes of the ovum, and seen how the embryo, the membranes and the reproductive cells are differentiated, we shall review in the next chapter the manner in which the ovum establishes itself in the cavity of the uterus and, for the space of 9 months, passes a parasitic life there.

NOTES AND REFERENCES

[1] See note on descent of testicle, p. 563.

[2] When the fimbriated end of the Fallopian tube is exposed in operations on the pelvis it is seldom found closely approximated to the ovary. Nevertheless it is probable that it is closely applied during the act of ovulation.

[3] For recent literature on the maturation, shedding and size of the human ovum, see Hamilton, W. J., *Jour. Anat.*, 1944, 78, 1; Simkins, C. S., *Amer. Jour. Anat.*, 1932, 51, 465 (treats of the human ovary from birth to maturity); de Thanhoffer, L., *Zeitsch. f. Anat. u. Entwickl.*, 1934, 102, 402; Evans and Swezy, *Amer. Jour. Physiol.*, 1931, 96, 628; Hill, Allen and Kramer, *Anat. Rec.*, 1935, 63, 239 (a film of the ripening and expulsion of the ovum of a rabbit).

[4] For evidence of the disappearance of early foetal ova, see Forbes, T. R., *Contrib. Emb.*, 1942, 30, 11; Stein and Allen, *Anat. Rec.*, 1942, 82, 1; the primary incursions carry ova to the medulla of the ovary, thus resembling the early incursions of the male gland.

[5] See Corner, G. W., *Yearbook of Carnegie Instit.*, 1944, p. 90; *Time of Ovulation in Women*, by C. G. Hartman, 1936. In *Macacus rhesus*, which is human in the length of its menstrual cycle, ovulation occurs between the 9th and 18th days (Hartman, C. G., *Contrib. Emb.*, 1932, 23, 1); see also Zuckerman and Parkes, *Proc. Zool. Soc. Lond.*, 1932, 141.

In most mammals ovulation occurs during the period of heat, rut or oestrus, which may be accompanied by a uterine discharge. Such discharge cannot correspond to the menstrual flow, for it occurs in the inter-ovulatory period. Oestrus in monkeys and apes of the Old World is made manifest by swelling and oedema of the external sexual parts.

[6] In *Macacus rhesus* the corpus luteum is fully developed 8 days after ovulation; if there is no pregnancy it passes into a state of degeneration before the 13th day; if pregnancy occurs it persists, assuming the "pregnancy" form after the 19th day, and reaches its maximum development by the 24th day. See Corner, G. W.,

Contrib. Emb., 1942, 30, 87. The observations that led to the discovery of the secretions or hormones formed in the corpora lutea have been summarized by Dr. Corner in the *Trans. Obstet. Soc. Edin.*, 1937, p. 61.

[7] For a statement of our knowledge of the functional relationships between pituitary and ovary, see Hartman, C. G., *Contrib. Emb.*, 1942, 30, 113; Thompson *ibid.*, 1937, e Gros and Allen, E.,

1932; Pfeiffer, C. A., *Amer. Jour. Anat.*, 1936, 58, 195; Billiter, Q. A., *ibid.*, 1936, 60, 357; Saxton and Loeb, *Anat. Rec.*, 1937, 69, 261; Gatz, A. J., *ibid.*, 1938, 70, 619; Clarke, Albert and Selye, *ibid.*, 1943, 83, 449. For chemistry of gonadotrophic hormones, see Freud, J., *Nature*, 1938, 141, 1014; Needham, J., *Biochemistry and Morphogenesis*, 1942, p. 176.

[8] For movements of spermatozoa and their survival in uterus, see Mann, T., *Nature*, 1945, 156, 80; Phillips and Andrews, *Anat. Rec.*, 1937, 78, 127; Parkes, G. H., *Phil. Trans.*, 1931, 219 (B), 381.

[9] It is now agreed that in mammals the first polar body is separated before the ovum is shed from its follicle, and that the second polar body is separated while the ovum is in the tube and about to be fertilized. See Hamilton, W. J., *Jour. Anat.*, 1944, 78, 1; Flynn, T. T., and Hill, J. P., *Trans. Zool. Soc. Lond.*, 1939, 24, 446 (ova of Monotremes). For size of pronuclei, see Mainland, D., *Jour. Anat.*, 1930, 64, 262; Hamilton, W. J., *ibid.*, 1936, 70, 429.

[10] For recent literature on chromosomes see Darlington, C. D., *The Evolution of the Genetic System*, 1939; *Nature*, 1942, 149, 66 (on chemistry of chromosomes); Waddington, C. H., *An Introduction to Modern Genetics*, 1939; *Organisers and Genes*, 1940; Goldschmidt, R., *Physiological Genetics*, 1938; Haldane, J. B. S., *Nature*, 1936, 137, 398; Koller, P. C., *Proc. Roy. Soc. Edin.*, 1937, 47, 194 (for sex chromosomes); de Winiwarter, H., *Archiv. Biol.*, 1938, 49, 111; Cowdry, E. V., *Text Book of Histology*, 1935; Roberts, J. A. Frazer, *An Introduction to Medical Genetics*, 1940.

[11] For structure and formation of spermatozoa, see *Human Embryology*, by Hamiton, Boyd and Mossman, 1945, p. 7; Froriep, E., *Anat. Anz.*, 1936, 82, 1.

[12] Spermatozoa are anaerobic if kept in a medium containing glucose; see Mann, T., *Nature*, 1945, 156, 80.

[13] For an account of the cleavage of the macaque ovum, see Lewis and Hartman, *Contrib. Emb.*, 1933, 24, 187; Wislocki and Streeter, *ibid.*, 1938, 27, 1 (changes after the 8th day); researches into the embryology of the rhesus monkey, made by workers of the Carnegie Institution, Washington, were issued in a special volume of *Contributions to Embryology* in 1941; human ova have been kept alive in culture medium by W. H. Lewis (*Bull. Johns Hopkins Hosp.*, 1931, 48, 368); segmentation of the rabbit ovum has been described by G. G. Pincus, *Proc. Roy. Soc.*, 1930, 107, 132; for respiratory exchange during segmentation, see *Biochemistry and Morphogenesis*, by J. Needham, 1942.

on

19 . . .

[14] Dr. Streeter announced the discovery of these two early embryos in the *Year Book of the Carnegie Institution, Washington* 1930 . . . these two embryos . . . 11th day the . . . Like . . . the monkey, the blastocyst of the . . . becomes completely embedded in the endometrium. An account of

the early human blastocysts have been published by Hertig, A. T., and Rock, J., in *Contrib. Emb.*, 1941, **29**, 127; 1945, **31**, 65. Heuser, Rock and Hertig, *Contrib. Emb.*, 1945, **31**, 85 (two embryos showing early stage of definite yolk sac). See also Hertig, A. T., in *Contrib. Emb.*, 1935, **25**, 37. Hertig and Rock, *Anat. Rec.*, 1946, **94**, 469 (an account of a four-day human blastula). Dr. G. W. Corner reported in the *Year Book of the Carnegie Institution* (Washington, 1943, p. 107) that the Institution had then at its disposal seven human blastocysts between the 7th and 12th days of development. Prof. F. Davies has published a preliminary account of one in the 10th day (*Nature*, 1944, **153**, 463).

[15] Accounts of human embryos in the 3rd week of development, in the presomite stage, have been published recently by: Odgers, P. N. B., *Jour. Anat.*, 1941, **75**, 381; Johnston, T. B., *ibid.*, 1941, **75**, 1, 153; George, W. C., *Contrib. Emb.*, 1942, **30**, 3; Gladstone and Hamilton, *Jour. Anat.*, 1942, **187**, 9; Florian and Hill, *ibid.*, 1935, **69**, 399; Heuser, C. H., *Contrib. Emb.*, 1932, **23**, 253; Kindred, J. E., *Amer. Jour. Anat.*, 1933, **53**, 221; Ramsey, Eliz. M., *Contrib. Emb.*, 1937, **26**, 101; Martin and Falkner, *Amer. Jour. Anat.*, 1938, **63**, 251; Shaner, R. F., *Canadian Jour. Research*, 1945, **23**, 235.

Accounts of human blastocysts late in the 2nd or early in the 3rd week have been published by: Hertig, A. T., and Rock, J., *Amer. Jour. Obstet. and Gyn.*, 1944, **47**, 149 (seven early human blastocysts are compared); Wislocki and Streeter, *Contrib. Emb.*, 1938, **27**, 1 (comparison of human and macaque blastocysts); Brewer, J. L., *Amer. Jour. Anat.*, 1937, **61**, 429; Stieve, H., *Zeitsch. Mikroskop. Anat. Forsch.*, 1936, **40**, 281; Dible and West, *Jour. Anat.*, 1941, **75**, 269.

[16] For literature on the primitive (Hensen's) node and formation of head process, see Florian and Hill, *Jour. Anat.*, 1935, **69**, 399; Heuser, C. H., *Contrib. Emb.*, 1932, **23**, 253; Kindred, J. E., *Amer. Jour. Anat.*, 1933, **53**, 321; Waddington, C. H., *Phil. Trans.*, 1932, **221** (B), 179; Assheton, R., *Quart. Jour. Mic. Sc.*, 1909, **54**, 221.

[17] Dr. G. L. Streeter* has done a signal service to embryologists by collating all data relating to human embryos undergoing the process of segmentation (4th week), *Contrib. Emb.*, 1942, **30**, 213. Specimens have been recently described by: Orts Llorca, *Zeitsch. f. Anat. u. Entwickl.*, 1934, **103**, 765 (4 somites); Boyd and Baxter, *Jour. Anat.*, 1938, **72**, 624 (10 somites); West, C. M., *ibid.*, 1937, **71**, 169 (25 somites). For variability of human embryos, see Grosser, O., *Zeitsch. f. Morph.*, 1934, **34**, 108.

[18] For literature on the origin and segregation of ova, see Forbes, T. R., *Contrib. Emb.*, 1942, **30**, 11; Stein and Allen, *Anat. Rec.*, 1942, **82**, 1; Hooker and Cunningham, *ibid.*, 1938, **72**, 371 (re-formation of testes of birds from peritoneal epithelium); Hamlett, C. W. D., *ibid.*, 1934, **61**, 273; Politzer, G., *Zeitsch. f. Anat. u. Entwickl.*, 1933, **100**, 331; Willier, B. H., *Anat. Rec.*, 1938, **70**, 89 (in chick embryos); Murotori, G., *Contrib. Emb.*, 1937, **26**, 61 (culture of germ cells).

* Dr. Streeter, lovable and able, died suddenly in the autumn of 1948 at the age of 75.

CHAPTER II

THE MANNER IN WHICH A CONNECTION IS ESTABLISHED BETWEEN THE FOETUS AND UTERUS

The Menstrual Cycle.—From puberty to menopause the sexual system of every woman passes through a recurring cycle of changes, each cycle lasting—according to the individual and her state of health—from 25 to 35 days, with a mean of 28. Cycles are timed and controlled by hormones secreted in the pituitary—gonadotrophic hormones, they are named. Clinicians date each cycle from the first day of menstruation, as this is the only event that has a definite outward manifestation. Each cycle may be divided into three phases. The first phase, which we may name the *menstrual* or destructive, lasts about 4 days; then follows the second or *follicular* phase, which extends to about the 15th day, when ovulation is due. During this phase a Graafian follicle is ripening in an ovary, while the mucous membrane (endometrium) of the uterus, having repaired the menstrual loss, is beginning to hypertrophy. In the phase just described the ovary and uterus are under the influence of a hormone formed in the ovarian follicle—oestrin. In the 3rd or *luteal* phase another hormone (progesterone) begins to affect both ovary and uterus. Progesterone, formed in the corpus luteum of an ovary, induces further growth in the endometrium with other changes in cervix and vagina. The luteal phase lasts from the day of ovulation to that in which menstruation recurs, a period that is usually one of 13 days. In the luteal phase both hormones are in circulation and are operative, but the luteal influence gradually becomes dominant. If impregnation does not occur, then a point is reached when the follicular hormone falls below a certain level, and at this point menstruation again sets in [1].

The Decidua.—As we have seen, the developing ovum reaches the cavity of the uterus about the 7th day, and on the 8th begins to embed itself. It finds the endometrium at the height of its luteal phase and prepared for its reception. To this hypertrophied state of the endometrium the name *decidua* is given. The *decidua*, which in the follicular phase has been thin, becomes thickened in the luteal phase to a localized mechanical mass. Three layers or strata are recognized in the decidua: a superficial or compact layer in which the contracted mouths of the uterine

the early human blastocysts have been published by Hertig, A. T., and Rock, J., in *Contrib. Emb.*, 1941, 29, 127; 1945, 31, 65. Heuser, Rock and Hertig, *Contrib. Emb.*, 1945, 31, 85 (two embryos showing early stage of definite yolk sac). See also Hertig, A. T., in *Contrib. Emb.*, 1935, 25, 37. Hertig and Rock, *Anat. Rec.*, 1946, 94, 469 (an account of a four-day human blastula). Dr. G. W. Corner reported in the *Year Book of the Carnegie Institution* (Washington, 1943, p. 107) that the Institution had then at its disposal seven human blastocysts between the 7th and 12th days of development. Prof. F. Davies has published a preliminary account of one in the 10th day (*Nature*, 1944, 153, 463).

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Accounts of human blastocysts late in the 2nd or early in the 3rd week have been published by: Hertig, A. T., and Rock, J., *Amer. Jour. Obstet. and Gyn.*, 1944, 47, 149 (seven early human blastocysts are compared); Wislocki and Streeter, *Contrib. Emb.*, 1938, 27, 1 (comparison of human and macaque blastocysts); Brewer, J. L., *Amer. Jour. Anat.*, 1937, 61, 429; Stieve, H., *Zeitsch. Mikroskop. Anat. Forsch.*, 1936, 40, 281; Dible and West, *Jour. Anat.*, 1941, 75, 269.

[16] For literature on the primitive (Hensen's) node and formation of head process, see Florian and Hill, *Jour. Anat.*, 1935, 69, 399; Heuser, C. H., *Contrib. Emb.*, 1932, 23, 253; Kindred, J. E., *Amer. Jour. Anat.*, 1933, 53, 321; Waddington, C. H., *Phil. Trans.*, 1932, 221 (B), 179; Assheton, R., *Quart. Jour. Mic. Sc.*, 1909, 54, 221.

[17] Dr. G. L. Streeter* has done a signal service to embryologists by collating all data relating to human embryos undergoing the process of segmentation (4th week), *Contrib. Emb.*, 1942, 30, 213. Specimens have been recently described by: Orts Llorca, *Zeitsch. f. Anat. u. Entwickl.*, 1934, 103, 765 (4 somites); Boyd and Baxter, *Jour. Anat.*, 1938, 72, 624 (10 somites); West, C. M., *ibid.*, 1937, 71, 169 (25 somites). For variability of human embryos, see Grosser, O., *Zeitsch. f. Morph.*, 1934, 34, 108.

[18] For literature on the origin and segregation of ova, see Forbes, T. R., *Contrib. Emb.*, 1942, 30, 11; Stein and Allen, *Anat. Rec.*, 1942, 82, 1; Hooker and Cunningham, *ibid.*, 1938, 72, 371 (re-formation of testes of birds from peritoneal epithelium); Hamlett, C. W. D., *ibid.*, 1934, 61, 273; Politzer, G., *Zeitsch. f. Anat. u. Entwickl.*, 1933, 100, 331; Willier, B. H., *Anat. Rec.*, 1938, 70, 89 (in chick embryos); Murotori, G., *Contrib. Emb.*, 1937, 26, 61 (culture of germ cells).

* Dr. Streeter, lovable and able, died suddenly in the autumn of 1948 at the age of 75.

The inner cell mass, from which the embryo will arise, projects within the cavity and is protected by the enveloping layer or trophoblast of the blastocyst, the whole ovum measuring about 0.25 mm. in diameter. Implantation usually takes place on the posterior wall of the cavity near the fundus of the uterus, but it may occur anywhere, that form being especially dangerous in which implantation occurs in the neighbourhood of the internal mouth of the cervix. The area of the trophoblast in contact with the decidua grows rapidly and throws off proliferating masses of syncytium (Fig. 19, p. 19), which burrow into the decidua,

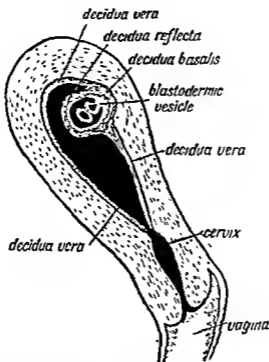


FIG. 28. Section of the Uterus showing in a diagrammatic manner the Embedded Ovum and the differentiation of the Decidua into Three Parts.

thus embedding and anchoring the blastocyst and, by the absorption of the decidual tissue, providing nourishment for it. The blastocyst is peculiar in man and the anthropoids in that it becomes completely buried in the decidua. The parts of the decidua are thus distinguished : (i) the *decidua serotina* or *basalis*, the part to which the ovum ultimately becomes attached and into which the processes of syncytium grow (Fig. 28); (ii) the *decidua capsularis* or *reflexa*, the part that covers the ovum and is stretched as the ovum grows; (iii) the *decidua vera*, which lines the rest of the uterus. The decidua vera ends at the internal os, the canal of the cervix producing no true decidual layer. With the growth of the embryo the decidua reflexa is brought in contact with the decidua vera. By the 5th month they have fused together, become

glands end; a thick intermediate or spongy layer containing irregular dilatations and elongations of the lumina of the glands; a bottom or basal layer, which abuts on the inner muscular coat of the uterus. In the decidual state all three constituents of the endometrium, glands, vessels and interglandular, are altered. The glands become elongated, branched and hypertrophied; in many mammals their secretion affords pabulum for the early embryo, but in man and anthropoids this supply has been rendered unnecessary by the early and profuse development of trophoblast. Certain cells of the interglandular stroma, especially in the compact stratum that underlies the epithelium, assume an epithelioid appearance, with relatively large cell bodies. These are known as

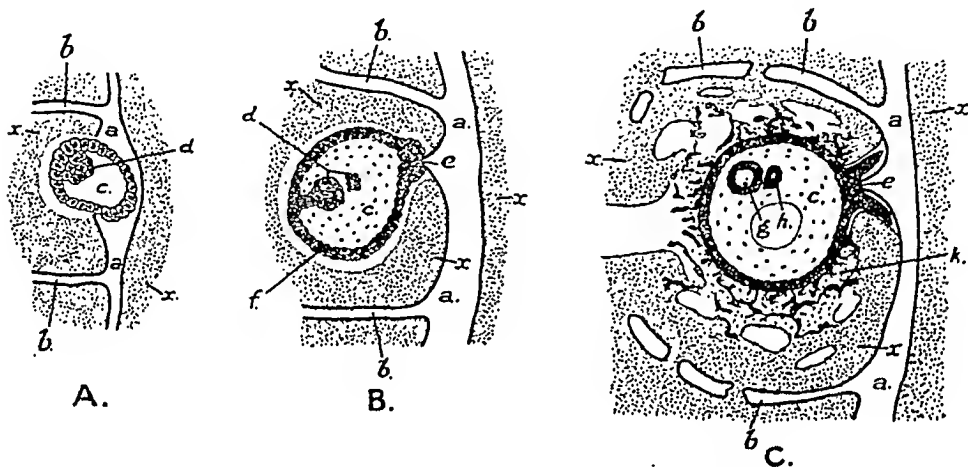


FIG. 27. Three stages in the implantation of the Human Ovum as represented by the late Prof. J. H. Teacher.

A. The blastocyst beginning to penetrate the mucous membrane of the uterus, the pole with the inner cell mass leading. The blastocyst is about 0.2 mm. in diameter and about the 7th day of development.

B. The blastocyst has become embedded in the decidua and the aperture of entry closed. About the 8th day.

C. The blastocyst towards the end of the 2nd week.

a, Cavity of uterus; b, uterine glands; c, cavity of blastocyst; d, inner cell mass; e, point of entry; f, enclosing trophoblast; g, cavity of amnion; h, cavity of archenteron; k, trophoblast and syncytium; x, decidua.

decidual cells and fall a prey to the invading trophoblast. The chief change, however, is that shown by the vascular constituents. Fine arteries, which ascend between the glands from the basal layer towards the compact stratum, have become elongated and coiled. The capillary network, lying in and under the compact layer, in which the coiled arteries terminate, undergoes so great a dilatation that they form sinus-like venous channels. In these venous sinuses, stasis of the blood takes place; there is interglandular oedema with an invasion of leucocytes. On penetrating the surface epithelium, the developing ovum finds awaiting it a free supply of nourishment in the decidua.

Implantation of the Ovum.—When the fertilized ovum reaches the cavity of the uterus it has already attained the blastocyst form (Fig. 27).

must examine the structures in the lower vertebrates from which the allantois has been evolved. These parts are represented in Fig. 31—depicting a condition found in *amphibia*. The rectum and also the ducts of the testes—the two Wolffian ducts—end in a terminal passage—the cloaca. An expansion or diverticulum of the cloaca has been established as a receptaculum for urine—the bladder. The blood supply is peculiar. A large vein passes along the inner aspect of the ventral wall of the belly, draining the blood from the bladder and from the ventral wall of the belly, as well as from the hind-limbs, and ending with the vein from the bowels and stomach in the portal system of the liver. Originally this ventral abdominal vein is double, there being a right and left vein, which convey the blood of the bladder and of the ventral wall (but not that of the limbs—the connection of the femoral veins is secondary) direct to the heart. The arteries that supply the bladder and ventral wall

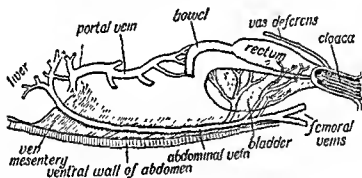


FIG. 31. The Cloaca, Bladder and Abdominal Vein of a frog.

spring from the common iliac arteries—these latter vessels representing direct continuation of the right and left primitive aortae. If, then, the allantois represents a precocious outgrowth from the apical region of the bladder and the chorion and amnion enormous and premature expansions from the ventral belly wall, we expect that their arteries should arise from the hinder ends of the embryonic aortae and their veins pass forwards on the body wall to terminate at first in the heart and afterwards in the liver. That is exactly what we do find, as may be seen from a reference to Fig. 29.

To see the allantois in its complete form one must examine the developing chick embryo (Fig. 32). The young of animals that are developed within a shell need a receptaculum for the secretion from their kidneys; for this reason alone one can understand the expansion of the embryonic bladder. But even in the chick its use as a store place for urinary excretions has become of minor importance; it is the mesodermal tissue clothing the bladder that has become the important element;

vitello-intestinal duct. Very soon after this, the duct closes and atrophies, but the sac itself continues to grow until it reaches a diameter of 4 or 5 mm. Its further history we shall examine later (p. 411), but here we may state that when the umbilical cord is fashioned the remains of the

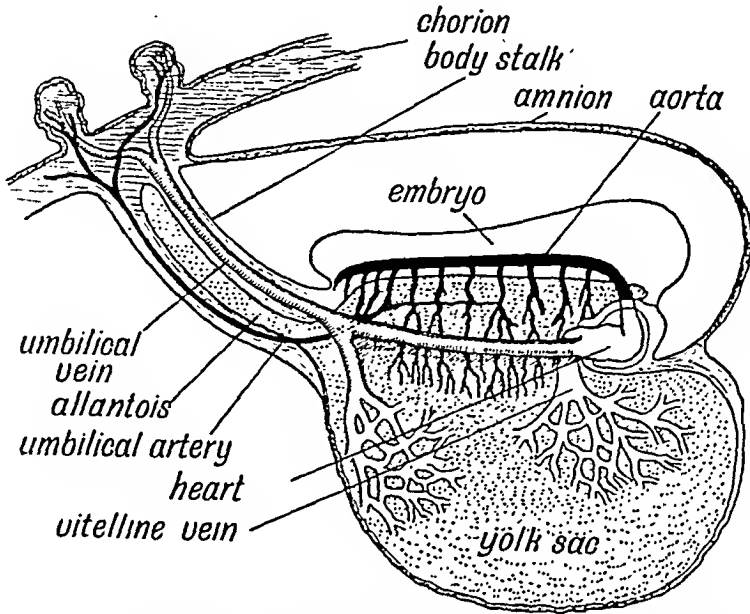


FIG. 29. The Yolk Sac and early vessels of the Human Embryo about the beginning of the 4th week of development. (Modified from Eternod.)

vitello-intestinal duct are enclosed within it, while the sac itself will be found at or near the placental end of the cord. In Fig. 30 is shown a section across a small part of the wall of the yolk sac to illustrate the manner in which embryonic blood corpuscles (erythrocytes or erythro-

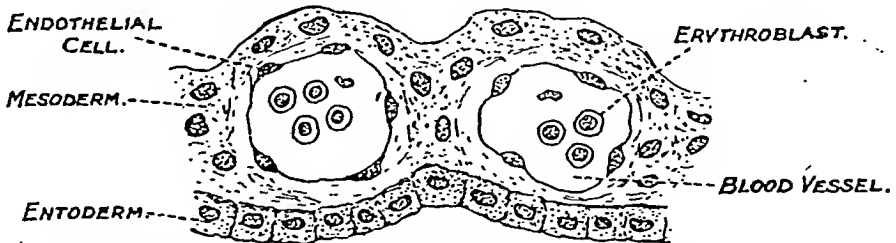


FIG. 30. Section across the wall of the Yolk Sac, showing blood-vessels and erythrocytes or erythroblasts forming in its mesoblastic layer. (After Selenka.)

blasts) and blood-vessels are formed in the mesodermal stratum of its wall. The lining endoderm also gives rise to glandular structures.

The Allantois.—The allantois appears during the 3rd week of development of the human embryo as an outgrowth from the hinder end of the archenteron or primitive gut cavity. To understand its true nature we

represents diagrammatic sections across chick embryos, the origin of the enveloping membranes is set out in a pictorial form. The somatopleure or body wall is seen to arise as a fold at each side of the embryo and mounting upwards ultimately to meet and fuse along the median dorsal line. The inner fold separates from the outer and forms the amnion; the outer remains as a membrane enveloping the embryo, amnion, yolk sac and allantois and is the basis of the chorion—the prechorion it is named in the chick. From the diagrams one would infer that the greater part of the chick's body wall was folded off to form the enveloping membranes, but when we remember that the yolk sac represents a

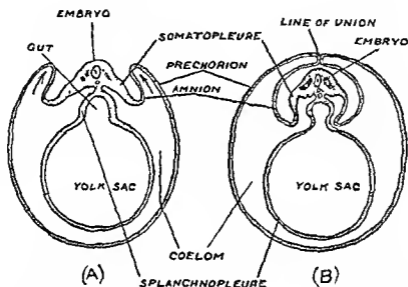


FIG. 33. Illustrating the manner in which the Chorion and Amnion arise in the Chick Embryo from folds of the Somatopleure—the body-wall of the Embryo. In A, the folds are seen in the act of growing upwards to cover the embryo; in B, they have met over the embryo.

premature but enormous development of a localized part of the howel, we may justly conclude that the enveloping part of the somatopleure represents a limited area of the ventral part of the abdominal wall—the part drained by the ventral abdominal vein—which has become greatly expanded. The assignation of part of the somatopleure to form the enveloping membranes involves no sacrifice of muscle or nerve in the belly wall of the embryo; we shall see that these elements invade the somatopleure long after the membranes have become separated from the body of the embryo. Only two elements of the belly wall have been utilized in the formation of the amnion and chorion: (i) the epithelial or ectodermal covering of the skin, which becomes the trophoblast; (ii) the mesodermal element, which gives rise to connective tissue, blood-vessels and blood cells. The villi of the chorion represent enormously

it has grown exceedingly rich in vascular tissue. As the allantois expands in the developing chick its vascular surface becomes applied to the inner aspect of the chorion, through which it can absorb oxygen and discharge carbon dioxide. The apical part of the bladder has thus become converted into a "foetal lung," but its vessels are those we have just noted in the ventral area of the frog; its arteries—the *umbilical arteries*—appear to be direct continuations of the two aortae, and its veins—the *umbilical veins*—pass to the heart and afterwards to the liver, just as in the frog.

~ In the human embryo, as is the case in all developing primates, the cavity of the allantois is never represented by more than a tubular outgrowth into the body stalk (see Figs. 20, 21 and 29), and even this degenerates very soon. The human embryo has no need for a bladder, as urinary excretion can be discharged into the maternal circulation as

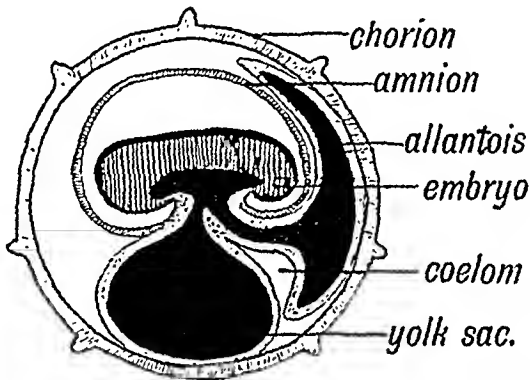


FIG. 32. The primitive form of the Allantois. (After Turner.)

soon as the placental circulation is established. It is otherwise with the mesodermal covering of the allantois; we shall see that this element, which has become amalgamated with the enclosing trophoblastic wall, takes the chief part in the vascularization of the chorion. In Fig. 29 it will be seen that the umbilical vein is connected with the vascular system of the yolk sac at the root of the allantoic diverticulum. We may regard the allantoic circulation as an enormous expansion from the more primitive circulation of the archenteron.

Evolution of the Amnion and Chorion.—If our knowledge were confined to the highly specialized processes that give rise to the amnion and chorion, the enveloping membranes of the human embryo, it would be almost impossible for us to guess that these structures represent, in reality, folds of the embryo's own belly wall. They come into existence before even the embryo itself is apparent. Their very humble but marvellous origin is illuminated when we examine the manner in which they arise in reptiles, birds and the lowest mammals. In Fig. 33, which

represents diagrammatic sections across chick embryos, the origin of the enveloping membranes is set out in a pictorial form. The somatopleure or body wall is seen to arise as a fold at each side of the embryo and mounting upwards ultimately to meet and fuse along the median dorsal line. The inner fold separates from the outer and forms the amnion; the outer remains as a membrane enveloping the embryo, amnion, yolk sac and allantois and is the basis of the chorion—the prechorion it is named in the chick. From the diagrams one would infer that the greater part of the chick's body wall was folded off to form the enveloping membranes, but when we remember that the yolk sac represents a

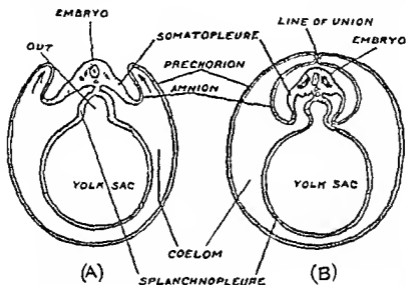


FIG 33. Illustrating the manner in which the Chorion and Amnion arise in the Chick Embryo from folds of the Somatopleure—the body-wall of the Embryo. In A, the folds are seen in the act of growing upwards to cover the embryo; in B, they have met over the embryo.

premature but enormous development of a localized part of the howel, we may justly conclude that the enveloping part of the somatopleure represents a limited area of the ventral part of the abdominal wall—the part drained by the ventral abdominal vein—which has become greatly expanded. The assignation of part of the somatopleure to form the enveloping membranes involves no sacrifice of muscle or nerve in the belly wall of the embryo; we shall see that these elements invade the somatopleure long after the membranes have become separated from the body of the embryo. Only two elements of the belly wall have been utilized in the formation of the amnion and chorion: (i) the epithelial or ectodermal covering of the skin, which becomes the trophoblast; (ii) the mesodermal element, which gives rise to connective tissue, blood-vessels and blood cells. The villi of the chorion represent enormously

overgrown villi of the cutis or true skin. Prof. J. P. Hill has demonstrated that in the developing marsupial ovum, when only 3 cell divisions have occurred and only 16 or fewer cells are formed, those which are to give rise to the epithelial covering of the chorion and amnion can be distinguished from the smaller number which is to form the embryo. In the human ovum it is also so ; we have seen that the epithelial covering of the chorion—the trophoblast—is the first structure to be differentiated in the development of the blastocyst. In prehistoric times primitive man required no scaffolding or machinery to build his rude hut ; in great modern buildings extensive scaffolding and elaborate machines have to be erected before ever building has begun. The chorion and amnion are the scaffolding thrown up for the development of the higher vertebrates, and they were evolved out of simple parts of the belly wall.

The amnion, which contains a fluid in which the embryo floats and thus has its very delicate growing tissues equally supported on all sides, is not required in the development of fishes or amphibians ; their eggs are hatched in water and the larvae live in water and have therefore no need of an amnion. This structure became necessary when the ancestry of the higher vertebrates took to a life on land. To allow their young to develop in the ancestral medium the amnion was evolved from a duplication of the embryo's body wall. Having thus given a clue to the evolutionary history of these marvels of adaptation—the amnion and chorion—we return to note stages by which the placenta is produced from the chorion and a foetal circulation established [6].

Chorionic Villi.—The origin of the chorion from a combination of two elements—the trophoblast (enveloping layer of ectoderm) and an inner stratum that represents somatic mesoderm—has been already traced (p. 18). The division of the trophoblast into a basal layer and syncytium was also mentioned. As soon as the ovum is embedded in the decidua, processes of syncytium invade not only the basal but also the reflected or capsular part (Fig. 27). Villi, containing a core of mesoderm and a covering of the basal layer of chorionic epithelium, grow out into the syncytial masses (Fig. 34). The villi, at first simple processes, begin to divide and re-divide in the 3rd week ; in the 4th, they become branched, and by the 30th day they are tree-like and fully formed. Hertwig [5] observed that the mesodermal core of villi may arise in situ by a direct transformation of the trophoblast. During the 3rd week the mesodermal tissue of the chorion, particularly of its villi, becomes the site of active formation of blood-vessels, blood cells being developed within the vascular lumina [5]. Similar formations are taking place in the body stalk, in the wall of the yolk sac and also in the embryo itself, so that by the middle of the 4th week a tubular heart, dorsal aortae,

vitelline and umbilical veins communicating with a great capillary network have been laid down (Fig. 29, p. 26). By the end of the 4th week a circulation of blood has been established in the chorion. Direct prolongations of the two dorsal aortae now extend through the body-stalk to the chorion—these extensions forming the umbilical arteries. The umbilical veins carry the blood from the chorion through the body-stalk to the embryonic heart. Through the chorionic circulation the embryo is nourished.

Formation of Placental Blood Spaces.—The decidual nutriment only affords a temporary supply. The maternal circulation is opened and placed at the service of the embryo in the following manner. As the blastocyst penetrates the decidua, its outer covering of trophoblast gives

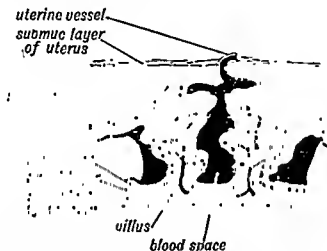


FIG. 34. Diagrammatic Section of the Decidua Serotina (formed from the mucous membrane of uterus) and Chorion, to show the manner in which the placental blood spaces are formed.

rise to massed hroods of cells—the syncytium—which demolish the surrounding decidual tissues and thus expand the space needed by the blastocyst (Fig. 27, C). The syncytium as it expands lays open minute vascular channels—both arterial and venous—and thus the maternal blood escapes into syneytial spaces; the blastocyst thus grafts itself on the maternal circulation. In the 3rd week villi begin to grow out from the outer wall or chorion into the syncytial masses. The masses of syncytium between the main villi break down and thus large spaces are formed into which the decidual vessels, which were enclosed by the syncytium, freely open (Figs. 27, 34). Through these spaces the maternal blood circulates, supplied by the uterine arteries and carried away by the uterine veins. The trophoblast contains a ferment which prevents coagulation of the blood in the intervillous spaces thus formed (Young). At the beginning of the 4th week the chorionic villi become

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two umbilical veins, and the canal of the allantois lie in its mesodermal basis, and while its upper ectodermal surface projects, like the rest of the embryo, within the cavity of the amnion, its lower surface lies in the wall of the extra-embryonic coelom, in contact with the yolk sac. The structures in the body-stalk are those which we find in the ventral belly wall of the frog (Fig. 31).

To understand the origin of the umbilical cord one must observe closely the attachment of the amnion at this early stage. It is attached to the circumference of the embryo and body-stalk (Figs. 22, 23, 24); to the zone of somatopleure which unites the embryo and the amnion the name of *junctional ring* may be given, with the clear understanding that the body-stalk enters into the formation of the posterior part of the ring. From the junctional ring the umbilical cord is developed. While the embryo grows rapidly and expands within the amnion the junctional ring expands very slowly. The parts of the yolk sac and coelom which are surrounded by the ring now appear to be constricted (Fig. 23). In the 2nd month the junctional ring begins to elongate and form a cord-like structure, in which an umbilical and a placental extremity can be recognized (Fig. 36). The amnion is attached at its placental extremity. The mesoderm of the junctional ring forms the jelly-like tissue (Wharton's jelly) of the umbilical cord in which are embedded the umbilical arteries and one umbilical vein, formed by the fusion of the right and left vein. By the 3rd month the cord measures 12 cm.; and 40 cm. by the 9th month. The elongation of the junctional ring to form the cord necessarily affects all those structures which lie within the ring—the neck of the yolk sac (vitello-intestinal duct), the coelomic space or primitive peritoneal space, the cavity of the allantois. All of these are included within the cord, and are obliterated during its elongation. From the 6th until the 10th week this space contains intestinal loops. The coelomic or peritoneal space at the umbilical end of the cord closes in the 3rd month, but if the intestinal loops fail to return it may remain open until birth and become the seat of a *congenital umbilical hernia*. As an exceptional occurrence, the intra-embryonic parts of the allantois or of the vitello-intestinal canal may remain patent as far as the umbilicus, and with the removal of the cord at birth give rise to a *urinary* or a *faecal fistula*.

Formation of the Placenta.—The condition of the membranes in the 3rd month (Fig. 36) differs from that of the 1st month (Fig. 21) by the differentiation of the placenta. In the 1st month the chorion is uniformly covered by shaggy villi, this being the permanent condition in low primates (Lemurs). In man the chorionic villi which project within the decidua basalis or serotina hypertrophy, while those within the decidua

vascularized and soon after are filled with blood propelled by the heart of the embryo. Thus in the placenta two hearts are at work—the maternal and foetal. The extension of the syncytium, the formation of villi and of blood spaces, go on until the 5th month. By that time the basal and syncytial layers of epithelium on the villi are replaced by a single flattened layer of cells, the villi thus becoming a vast meshwork of fine vascular channels enclosed by a thin cellular covering derived from the original trophoblast. If we conceive the capillary network of a miniature lung as stripped from the alveoli, but retaining its mesothelial coating, we have before us a picture of a placental villus. The villi are gills, but are suspended in pools of oxygenated blood instead of oxygenated water. They are immersed in blood spaces, and draw

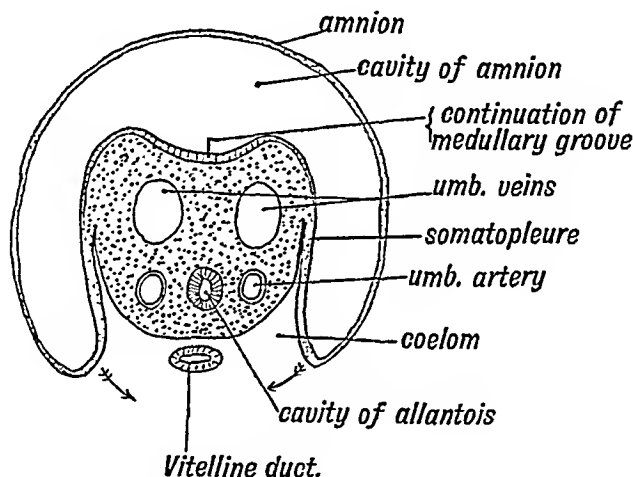


FIG. 35. Section across the Body-Stalk. (His.)

from the maternal blood oxygen and nutriment for the supply of the embryo. Processes and fibrinous partitions derived from the syncytium remain to bind the chorion to the uterine wall and to separate the villi into groups or cotyledons (see Fig. 38).

Formation of the Umbilical Cord [6].—At the end of the 3rd week of development (see Figs. 20, 29), when the embryo forms a cap on the yolk sac and a plate in the floor of the amniotic cavity, neither umbilicus nor umbilical cord is differentiated. The *body-stalk* unites the caudal end of the embryo to the inner wall of the chorion, and has the appearance of being a posterior extension of the embryonic body. Indeed, at an early stage the hinder end of the primitive streak lies on it (see p. 52), but the part which is to enter into the formation of the umbilical cord really represents a reflection of the ventral wall of the body. The body-stalk serves the purposes of an umbilical cord to the early embryo. A section across the body-stalk (Fig. 35) shows that two umbilical arteries,

3rd. An allantoic element which is fused with the mesoderm of the chorion in the human ovum. In the human placenta it is impossible to distinguish the 2nd from the 3rd element; both are fused in the mesoderm of the chorion from the beginning.

4th. The amnion, which becomes applied to the inner surface of the chorion, thereby obliterating the extra-embryonic coelom (Figs. 36, 37). Thus it will be seen that almost the entire placenta is produced from the ovum and is truly a part of the foetus. The decidua, the only maternal element, merely affords a nidus or suitable bed for the development of the foetal structures.

From the inner surface of the fully formed placenta, the amnion, a thin

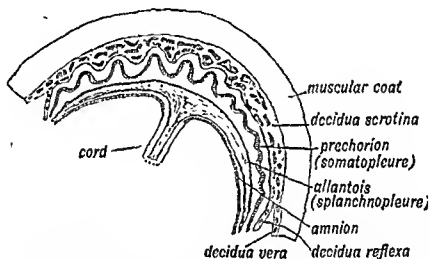


FIG. 37.—Diagrammatic section to show the elements which enter into the formation of the Placenta. The trophoblast on the outer side of the prechorion has been omitted for the sake of simplicity.

transparent membrane, is easily stripped off. The outer or uterine surface of the placenta is rough and shaggy, being mainly composed of the greatly hypertrophied villi developed from the serotinal or attached area of the chorion. The villi are grouped in clumps or cotyledons, between which are fibrous strands and partitions which pass through the whole thickness of the placenta and thus maintain its fixation to the uterus. The manner in which the trophoblast covering the villi becomes changed until it forms merely a thin epithelial covering has been already mentioned (p. 42). Into the villi pass branches of the umbilical arteries, ultimately forming a fine capillary network, from which the arterialized blood is returned to the foetus by the umbilical veins. Everywhere the blood of the foetus is separated from that of the mother by a thin capillary wall and a layer of flat epithelial cells; through this wall exchanges between the foetal and maternal circulation take place. The villi

reflexa atrophy, and in this way the discoidal placenta of man is formed (Fig. 36). In lower primates (Monkeys) the placenta may be bidiscoidal, one disc being formed at the embryonic pole of the blastocyst as in man, the other being produced at the opposite or vegetative pole [7]. The bidiscoidal form occurs occasionally in human pregnancies.

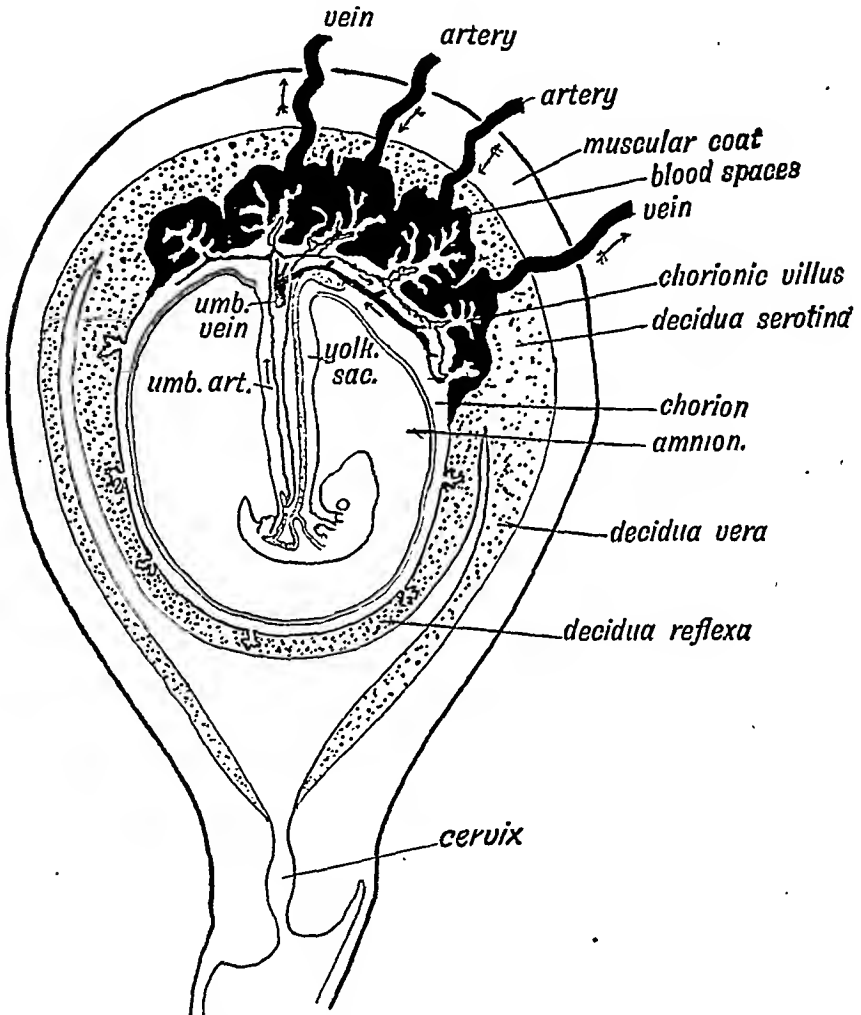


FIG. 36. Showing the arrangement of the Amnion, Chorion, and Decidua in the 3rd month and the formation of the Placenta.

The elements entering into the formation of the placenta are diagrammatically shown in Fig. 37. They are :

1st. The decidua serotina, formed by the mucous membrane of the uterus. It is almost completely replaced by the syncytium and chorionic villi. Only the basal layer with the bottom parts of the glands remain to furnish a new lining to the uterus when the membranes and placenta are shed after the birth of the child.

2nd.. The chorion, or, strictly, prechorion.

into the placental blood spaces (*g, g*). These blood spaces are occupied by the villous network (*f*). For diagrammatic effect some of these spaces are represented as empty. One partition has only the stumps of vessels attached to it (*c'*). The channels which perforate the basal layer represent the fine spiral arteries which supply the endometrium; through them the mother's heart fills the placental spaces with arterial blood. After bathing the villous network, the maternal blood, now in a venous state, flows towards the marginal spaces and makes its exit by the marginal maternal veins (*o, o*). Maternal blood can pass from space to space; as shown in Fig. 38, the partitions between spaces are perforated (arrows pass from *g* to *g'*). Thus the placenta is divided by partitions into a series of compartments or spaces, varying in number from 15 to 30. The villous mass which fills a compartment is known as a cotyledon. Since the compartments lie within the muscular wall of the uterus, every contraction of that wall tends to compress the placental blood-spaces, and so empty them into the uterine veins. The respiratory movements of the body wall have a similar effect.

At full term all the membranes of embryonic origin come away in the after-birth; also the decidua, except a thin, deep layer next the uterine muscle, which contains the deepest parts of the uterine glands. The removal of the placenta leaves a deep and extensive ulcer in the endometrium. Repair, as in an ordinary ulcer, is effected chiefly from the circumference, but the surviving tissue in the floor of the ulcer also shares in the repair, which is effected in about 25 days.

The establishment of the developing ovum within the uterus of the mother constitutes one of the most marvellous chapters of Embryology. It is apparent that in the evolution of the higher mammals the young have become modified to pass the first stage of life as uterine parasites. In this chapter we have seen that the ovum has already reached a certain degree of development when it enters the uterus from the Fallopian tube. All the earlier steps in development are directed towards the formation of the structures necessary for the protection of the embryo—the chorion, amnion, yolk sac, allantois and placenta.

NOTES AND REFERENCES

- [1] Since 1930 the literature on the menstrual cycle in women and the part played by the pituitary and other glandular structures in regulating the functions of uterus and ovaries by hormones has assumed enormous proportions. Some of the publications I have used have been cited in notes 5, 6, 7 appended to the preceding chapter. Here I add a few more: Aron, Max, *Archiv. d'Anat.*, 1932, 15, 243 (Summary of research on gonadotropic hormones up to 1932); Klein, M., *ibid.*, 1936, 18, 1-142 (effects of excision of corpus luteum); Robson, J. M., *Recent Advances in Sex and Reproductive Physiology*, 1934; Hartman, C. G., *Anat. Rec.*,

project within great blood spaces formed from the maternal sinuses. The ovarian and uterine arteries end in these blood sinuses, and the ovarian and uterine veins begin in them (Fig. 38).

Structure of the Placenta.—In Fig. 38 is reproduced a semi-diagrammatic representation of the fully formed placenta, according to the description given by Spanner [9]. The termination of the umbilical cord is shown (*a*); a branch (*b*) of the umbilical artery, carrying the venous blood from the foetus, is shown under the amnion (*i*) and amniotic surface of the chorion (*k*); it sends a branch down a partition (*c*)

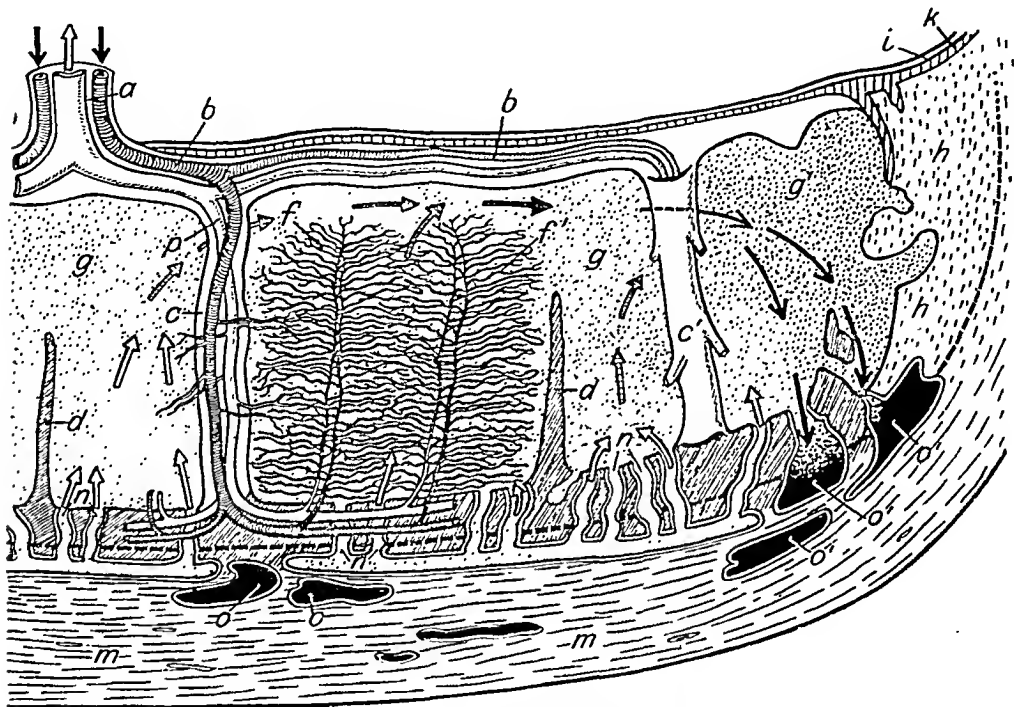


FIG. 38. A Semi-diagrammatic section of the fully developed Human Placenta. (After Spanner.) Only a single segment is depicted. For explanation, see text. The arrows show the direction of the flow of maternal blood.

towards the basal layer, resting on the inner muscular coat of the uterus (*m, m*). On reaching the basal layer, chorionic arteries are reflected towards the amniotic surface. There they open into complex vascular channels (*f*), and are attached to neighbouring septa (*d*). The veins (*p*) which now receive the arterialized blood from the network ascend in the partitions and unite with others under the amniotic surface of the placenta, and so give rise to umbilical veins.

Such are the foetal structures connected with placental circulation. Let us now enumerate the structures concerned in the maternal circulation. It will be noted that the basal layer of the placenta is pierced at numerous points by small spiral arterial channels (*n, n, n*) that open

J. Zell. Forsch. u. Mik. Anat.,

ges in human placentation, see

Dr. J. D. Combs has recon-

structed the endometrial nest of a human blastocyst of the 13th day (*Anat. Rec.*, 1941, 81, 265).

[8] The recuperative power of the endometrium is illustrated by an experiment by C. G. Hartman on a female rhesus monkey. He removed the endometrium completely; in the course of 13 days it was restored and became the site of a successful pregnancy.

[9] For structure of placenta and of endometrium, see Spanner, R., *Zeitsch. f. Anat. u. Entwickl.*, 1936, 105, 163; Grosser, O., *Lancet*, 1933, 1, pp. 999, 1053, 1055 (types of mammalian placentae); Stieve, H., *Anat. Anz.*, 1936, 81, 33 (Suppl.); Dees-Mattingly, H., *Amer. Jour. Anat.*, 1936, 59 (dimensions of absorptive area); Williams, J. W., *Amer. Journ. Obstet. Gynaec.*, 1931, 22, 664 (repair of endometrium after parturition); for structure of endometrium, see Daren, C. H., *Amer. Jour. Anat.*, 1936, 58, 349; Bartelmez, G. W., *Contrib. Emb.*, 1933, 24, 143; Markee, J. E., *Anat. Rec.*, 1938, 70, 54 (suppl.); Bacsich and Smout, *Jour. Anat.*, 1938, 72, 358 (structure of arteries); Mossman, H. W. (see reference under note [7]).

1938, 70, 35 (Suppl. 3); Zuckerman, S., *Proc. Roy. Soc.*, 1937, 125 (B), 441; 1938, 124 (B), 150 (cause of menstruation); McKeown and Zuckerman, *ibid.*, 1938, 124 (B), 464 (effect of gonadotropic hormones on rats); Markee and Others, *Anat. Rec.*, 1935, 64, 131 (endometrial grafts in eye); Corner, G. W., *Trans. Edin. Obstet. Soc.*, 1937, p. 61 (action of luteal hormone); Nicol, T., *Trans. Roy. Soc. Edin.*, 1935, 58, 449; *Jour. Anat.*, 1936, 70, 200 (action of oestrin on decidua of guinea-pig); Gardner, W. U., *Anat. Rec.*, 1937, 68, 339 (effects of oestrin); Hirsaw and Others, *Amer. Jour. Anat.*, 1937, 61, 483 (action of follicular and luteal hormones on endometrium of apes).

For observations on the cyclical changes in vagina, see Papanicolaou, G. N., *Amer. Jour. Anat.*, 1933, 52, 415; Smith and Brunner, *ibid.*, 1934, 54, 27. For changes caused by oestrin in the newly born: Fraenkel and Papanicolaou, *Amer. Jour. Anat.*, 1938, 62, 427; Zuckerman, S., *Jour. Anat.*, 1938, 72, 352. For observations on the menstrual cycle of apes, Hartman, C. G., *Contrib. Emb.*, 1932, 23, 1 (28 days in rhesus monkey); Zuckerman, S., *Proc. Zool. Soc. Lond.*, 1937, (1), 315; Elder and Yerkes, *Proc. Roy. Soc.*, 1936, 120 (B), 409; *Anat. Rec.*, 1937, 67, 119 (35-day cycle in chimpanzee); Schultz and Snyder, *Bull. Johns Hopkins Hosp.*, 1935, 57, 193.

[2] For substances formed in endometrium for use of embryo, see Rossman, I., *Amer. Jour. Anat.*, 1940, 66, 277; 1942, 69, 187 (in rhesus monkey); Nicol, Thos., *Journ. Anat.*, 1932, 66, 183.

[3] See G. L. Streeter, *Anat. Anz.*, 1938, 70, 53 (Suppl.).

[4] In seeking to discover the manner in which the evolution of the human body has been brought about, we have to recognize two phases of existence, an intra-uterine or parasitic phase and an extra-uterine or independent phase. It is during the intra-uterine phase that nearly all revolutionary changes in structure have been introduced. The time sequence in which parts are developed may be speeded up or they may be retarded. The precocious development of part of the intestine to form the yolk sac (archenteron), of the bladder to form the allantois, and of part of the abdominal parietes to form the amnion and chorion are extreme examples of precocious development, for these structures are differentiated before the body of the embryo is manifest. How such speeding-up is brought about we do not know. Another kind of transference in time or rate of development is even more important for the understanding of human evolution. Characters which made their first appearance during intra-uterine life may be retained after birth and may become characteristics of the adult. For example, man's large brain, small face and comparatively nude skin may be regarded as acquired from intra-uterine life. The tendency for foetal characters to be retained after birth is sometimes spoken of as Bolk's Law (see Keith, A., *Concerning Man's Origin*, 1927.)

[5] For earliest formation of blood-vessels in human embryos, see Hertig, A. T., *Contrib. Emb.*, 1935, 25, 37; Wislocki and Streeter, *ibid.*, 1938, 27, 1; Ramsay, Eliz. M., *ibid.*, 1938, 27, 69; Brewer, J. I., *ibid.*, 1938, 27, 87; Odgers, P. N. N. B., *Jour. Anat.*, 1937, 71, 161; McIntyre, D., *Trans. Roy. Soc. Edin.*, 1926, 55, 77.

[6] For a description of early stages in the development of human amnion and umbilical cord, see references given in the preceding note [5], to Hertig, A. T., and to Wislocki and Streeter; Wyburn, G. M., *Jour. Anat.*, 1939, 73, 289 (a detailed and original account of formation of the umbilical cord and of the umbilical region of the body wall); Mélke, J., *Anat. Anz.*, 1933, 76, 194 (changes in the umbilical artery).

[7] For an account of the placentation of man and apes, see Hill, J. P., *Phil. Trans.*, 1932, 221 (B), 45; for a comparative study of placentation, see Mossman H. W., *Contrib. Emb.*, 1937, 26, 133; for physiology of the placenta, see Barcroft, Sir J., *Proc. Roy. Soc.*, 1935, 118 (B), 242; Needham, J., *Biochemistry and Morphogenesis*, 1942, p. 79; Weekes, H. C., *Proc. Zool. Soc. Lond.*, 1935, p. 625

continuous with the ectoderm on the dorsal surface of the plate, the cavity of the primitive gut thus opening or having a mouth on the dorsal surface of the embryo (Fig. 39, *B*). If a section be made further back,

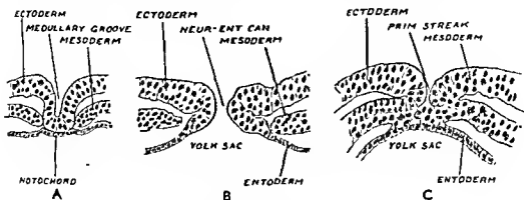


FIG. 39. Section across a human Embryonic Plate measuring 1.5 mm. in length. (Graf Spee) Notochord = Notochordal plate.

A. In front of the neurenteric canal.

B. At the neurenteric canal.

C. Across the primitive streak, behind the neurenteric canal.

across the region of the primitive streak (Fig. 39, *C*) it is seen that the endoderm fuses with the ectoderm and that, at the line of fusion the mesodermio plates are continuous with both endoderm and ectoderm—

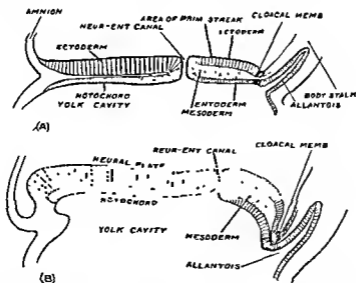


FIG. 40. Sections along the median line of two Embryonic Plates, figured by Graf Spee, to show the shifting backwards of the neurenteric canal and primitive streak as growth takes place.

but chiefly with the ectoderm. Along the streak there is a vigorous production of mesoderm, mainly from the ectoderm. A section in front of the neurenteric canal (Fig. 39, *A*) shows still other appearances:

CHAPTER III

THE PRIMITIVE STREAK, NOTOCHORD AND SOMITES

Law of Recapitulation.—The pioneers of Embryology began in the hope of discovering the stages in the evolution of the human body by an accurate study of its development. It was expected that the ovum as it became transformed into the embryo, and the embryo as it changed into the foetus would recapitulate man's evolutionary history. From what has been related in the two previous chapters it is plain that we see no resemblance between the successive stages of the human embryo and the succession of types which compose the scale of the Animal Kingdom. Those who expected the law of recapitulation to hold true in all its details forgot that the human embryo is radically modified in order that the first nine months of development may be spent parasitically in the womb of the mother. The storage of yolk in the ovum, the precocious development of trophoblast, chorion, amnion and allantois, have transformed the orderly manifestation of evolutionary stages. Yet to a certain degree the law remains true: the human body begins as a single cell, similar in constitution to the simplest form of animal life—a protozoon; it becomes a globular cluster of cells in its morula stage, similar to the simple forms of multicellular organisms. Further, there are numerous features seen during the development of the embryo which can only be explained by supposing that the human body, in the course of its evolution, has passed through those stages which we see represented in simpler Invertebrate forms—such as the Hydra and the worm. The first of these obscure embryonic manifestations is the primitive node and streak.

The Primitive Streak.—In the 3rd week, when the embryonic plate lies on the upper surface of the yolk sac and measures less than 1 mm. (1/25 in.) in length, there appears along the median line of its hinder half a linear demarcation known as the primitive streak (Fig. 20, p. 21). This line becomes the site of developmental processes of the highest significance. It indicates what is to be the mean longitudinal axis of the trunk. Very soon after the primitive streak appears there is formed a perforation or canal at its cranial or anterior end—the *neurenteric canal* (Fig. 40, A). If a section is made across the embryonic plate at the site of the canal, the endoderm lining the archenteron is seen to be

coming to enclose the neurenteric canal and anterior end of the primitive streak (Fig. 42). The early relationship of the medullary folds to the primitive streak is shown diagrammatically in Fig. 41. The hinder

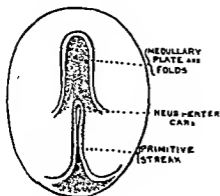


FIG. 41.

FIG. 41. Diagram of the Embryogenic area of an Embryonic Plate viewed from above.

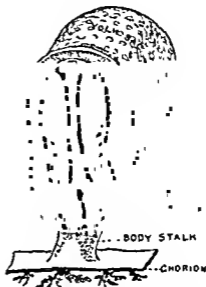


FIG. 42.

FIG. 42. The Medullary Plate and Primitive Streak of an Embryo at the beginning of the 4th week. (After Orst Spec.)

end of the streak is carried away from the cloacal membrane by the formation of the tail.

Hensen's Node and the Prechordal Plate [1].—We took up the consideration of the primitive streak late in the 3rd week after the neuren-

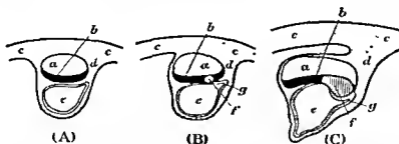


FIG. 43. Sagittal sections of Human Embryos in the 3rd week of development. (Dr. J. Florian)

A. Peter's ovum, about 15 days. B. Mollendorff's ovum. C. Florian's ovum, B I. a, Cavity of amnion; b, embryonic or ectodermal plate, c, c, chorion, d, body-stalk, e, archenteron; f, primitive streak; g, allantois.

teric canal had been formed at its anterior or cranial end. There are certain earlier stages which we must now glance at. In Fig. 43 diagrammatic sections of three human embryos are represented; in A, the

the ectoderm, now being differentiated into the neural plate, is moulded to form the rudiment of the medullary furrow; beneath the furrow there is a plate of cells, the *notochordal plate* (Fig. 39, *A*), which although continuous with the endoderm is yet of different origin. The notochordal plate will form the *notochord*, the supporting or skeletal rod of the medullary plate. At the neurenteric canal and in front of it the mesoderm is no longer continuous with the ectoderm or endoderm; it has grown forwards from the site of production at the primitive streak.

If sections are made along the embryonic plate (Fig. 40, *A* and *B*) further light is thrown on the relationship of the neurenteric canal and primitive streak to the growth of the embryo. In Fig. 40, *A*, the neurenteric canal is seen to be placed near the middle point of the plate, which has a total length of a little over 1 mm.; while in the older embryo, which measures 1.7 mm. in length, it has been pushed backwards by the rapid growth and extension of the precanalicular part of the embryonic plate. The region of the primitive streak—the postcanalicular part of the embryonic plate—although the site of mesodermal production, has undergone a lesser degree of growth and is being pushed to the hinder end of the embryonic plate. The exact manner in which the precanalicular part expands we shall describe presently, but in the meantime it may be noted that at the anterior lip of the neurenteric canal the ectodermal plate is in continuity with the notochordal plate. This lip, which represents the dorsal lip of the *blastopore*, and the adjacent parts of the primitive streak represent an actively growing bud which is to give rise to the greater part of the body of the embryo. The first formed part of the precanalicular plate represents the hinder cranial region; as the plate grows the neurenteric canal moves backwards through the cervical and dorsal regions until it reaches the lumbar region late in the 4th week, the embryo then being less than 3 mm. in length. If, as sometimes occurs, the neurenteric canal remains unclosed, a fistula from the bowel opens in the lumbar region of the spinal cord. In Fig. 40 it will be seen that while the neurenteric canal lies at the anterior end of the primitive streak a very important structure—the *cloacal membrane*—marks its posterior end. The cloacal membrane, extending to the dorsal surface of the body-stalk, marks the site of the anus and vulval cleft. Thus the greater part of the human body is developed by the anterior end of the primitive streak, a relationship which must be understood if certain malformations of the human body are to be adequately explained.

In the 3rd week of development, when the primitive streak is being pushed backward on the embryonic plate, the medullary folds appear on its anterior part, the hinder ends of the folds as they spread backwards

the cloacal membrane fills up the hinder end of the primitive streak and rests on the roof of the allantoic diverticulum.

Later History of the Primitive Streak.—It will be well to mention here the later history of the primitive streak. In Fig. 45 a sagittal section of the hinder half of a human embryo is depicted [2]; it is some 22 or 23 days old; eight segments have been demarcated—namely three occipital and five cervical. The hinder end of the embryonic plate has now become folded, so that the cloacal membrane, representing the hinder end of the primitive streak, lies on the under surface of the projecting caudal end of the plate. The anterior end of the streak, represented by

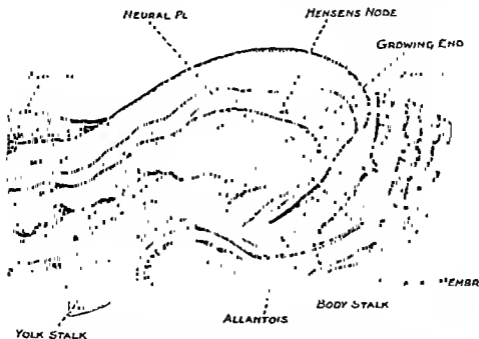


FIG. 45. Sagittal section of the hinder half of a Human Embryo in the earlier half of the 4th week of development. (Prof. Cecil M. West)

Hensen's node (Fig. 45), has now reached that part of the embryonic plate which in due time will be the site of the 5th cervical segment. The notochord and great neural plates anterior to the site of Hensen's node are already demarcated; all that part of the trunk which lies behind the 5th cervical segment has still to come into existence. Hensen's node and the tissues in its vicinity are to give rise to them in orderly sequence. The neurenteric canal has disappeared. The primitive streak is now included in the hinder end of the embryonic plate; the hinder end of the plate represents a germinal bud or centre of growth which gives rise not only to notochord, medullary plates, bone, muscle, pronephros and mesonephros and connective tissues, but also to an extension of the adjacent region of the archenteron. Part

ectoderm on the embryonic plate is represented by a thick black line; no clear sign of the primitive streak is detectable. In Fig. 43, *B*, it has become apparent; part of the ectodermal plate begins to grow and changes its character; it is the first trace of the primitive streak. In Fig. 43, *C*, a stage later in the 3rd week is shown, the streak area is elongating with the ectoderm of the cloacal plate at its hinder end and the unchanged cranial ectoderm in front.

In Fig. 44 sagittal sections of two ova late in the 3rd week of development are represented. In *A* certain changes in the primitive streak have to be noted. There is first its further extension backwards; secondly, at its anterior end, where the ectoderm is growing rapidly, a forward ingrowth over the roof of the archenteron has taken place. The raised

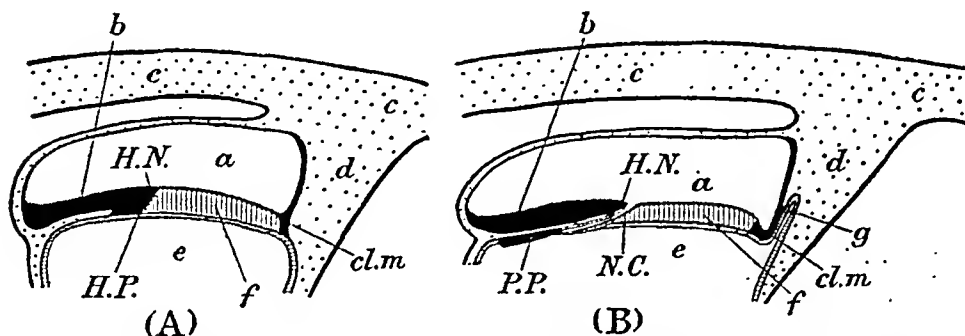


FIG. 44. Sagittal sections of two Human Embryos showing the production of the chordal or head process (*A*); and the formation of the neurenteric canal in that process (*B*). (Dr. J. Florian.)

a, Amniotic cavity; *b*, embryonic or ectodermal plate; *c*, *c*, chorion; *d*, body-stalk; *e*, archenteron; *f*, primitive streak; *g*, allantois; *cl. m.*, cloacal membrane; *H.N.*, Hensen's node; *H.P.*, head process; *N.C.*, neurenteric canal; *P.P.*, prechordal plate.

anterior lip of the streak, from which the ingrowth has sprung, is known as the *primitive* or *Hensen's node*; the ingrowth is named the *chordal* or *head process*. We are witnessing the laying down of the anterior end of the notochord. Now in the foetus the anterior end of the notochord lies within the base of the skull, extending from the pituitary fossa to the foramen magnum. The neuro-vertebral axis, therefore, begins its formation in the post-pituitary region. In Fig. 44, *B*, which represents a later stage, further changes have occurred. The chordal process has become canaliculized; the floor of the canal has disappeared, the neurenteric canal being thus formed. The roof of the canal becomes the chordal plate—the basis of the notochord. The endoderm in the roof of the archenteron, just in front of the chordal process, thickens and forms a plate—the *prechordal plate* (Fig. 44, *B*). Later, the prechordal plate, having given off mesoderm to the pre-pituitary region of the head, becomes included in the anterior end of the fore-gut. The ectoderm of

situated Hensen's node, from which the chordal or head process is being given off. A day or two later, Hensen's node has grown backwards, more of the chordal plate having been formed (Fig. 46, C). In front of the chordal process has appeared the prechordal plate. From this structure, as we have already seen, arises the mesoderm of the head.

Thus the trophoblast of the membranes and the hinder end of the primitive streak are the first sources of mesoderm. The final and greatest source is the primitive streak itself; along its whole length ectoderm is being rapidly transformed into mesoderm. As produced it passes inward to lie on each side of the elongating notochord, forming the bases of vertebrae, muscles, vessels and ligaments.

The Blastopore.—The primitive streak, with Hensen's node at its

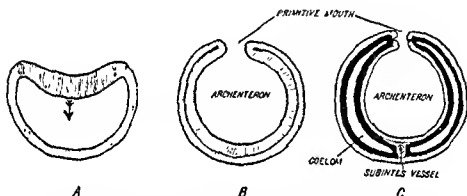


FIG. 47. Diagram showing three stages in the early development of *Amphioxus*.

A. Invagination of the endoderm (shaded) within the ectoderm (stippled).

B. Formation of archenteron and primitive mouth (blastopore).

C. Origin of mesoderm (black) and coelom from margin of primitive mouth, with formation of a ventral mesentery round the subintestinal vein. (After Robinson.)

front end and the cloacal membrane at its hind, can be most reasonably explained by supposing that it represents the primitive mouth or blastopore of lower invertebrate animal types. Its formation in the vertebrate body is best studied in *amphioxus* (Fig. 47). At an early stage of its segmentation the ovum of this animal forms a hollow sphere (Fig. 47, A); one part of the sphere becomes invaginated to form the endoderm, the uninvaginated or outer layer becoming the ectoderm. The brim of the bilaminar flask (gastrula or cup) thus formed serves as a mouth or blastopore to the cavity of the endoderm (archenteron, Fig. 47, B). The primitive streak, seen in all vertebrate embryos, is believed to arise from a linear fusion and backward growth of the lips of the blastopore. In the developing *amphioxus* mesoderm is seen to arise in the circular lip of the blastopore; in embryos of higher vertebrates it is seen to arise in the primitive streak, the representative of the

of the germinal bud may persist at the caudal end of the foetus and give rise to a large *sacro-coccygeal cyst* or tumour.

Origin of the Early Mesoderm.—We have seen that in the earliest human embryo known, mesoderm already covers the outer aspect of the archenteron and the inner aspect of the chorion. This mesoderm is derived from the trophoblastic foundations of the chorion, of the amnion, of the yolk sac and of the body-stalk, all of which represent precociously developed parts of the body wall and of the primitive gut. We have now to touch upon another and important source of mesoderm. It begins to be produced at the end of the 2nd week from that part of the embryogenic plate which is to become the hinder end of the primitive

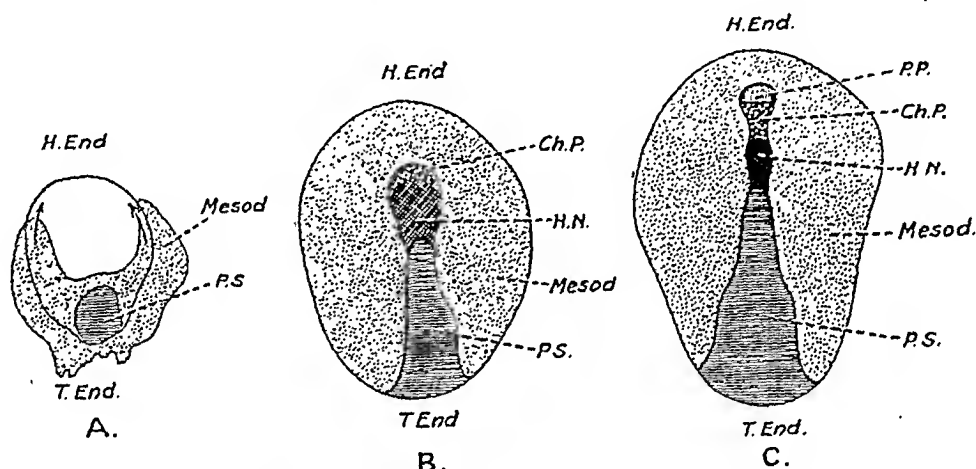


FIG. 46. The differentiation of the Primitive Streak in the Embryonic plate of the pig. *A.* Middle of the 2nd week. *B.* Early in the 3rd week. *C.* About the middle of the 3rd week. (G. L. Streeter.)

Mesod., mesoderm; *P.S.*, primitive streak; *H.N.*, Hensen's node; *Ch. P.*, chordal plate; *P.P.*, prechordal plate; *H. End.*, head end of embryonic plate; *T. End.*, tail end of embryonic plate.

streak. Its origin has been followed in the embryo of the pig by Dr. G. L. Streeter [3]. In Fig. 46, *A*, is represented the embryonic plate of a pig's embryo about 10 days old; it rests on the archenteron. The primitive streak has appeared. At its tail end and at its sides mesodermal cells are being formed and are spreading outwards on the archenteron and forwards, in a bicrescentic formation, in the embryonic plate (Fig. 46, *A*). The tips of the crescents meet at the cranial margin of the embryonic plate. In this early mesoderm, which forms much of the body-wall, vascular tissues arise; in its crescentic tips the basis of the heart will be formed. Also from the hinder end of the primitive streak arises mesoderm which passes into the body stalk on each side of the cloacal membrane; this tissue goes to the formation of the infra-umbilical part of the body wall. A day or two later (Fig. 46, *B*) the primitive streak has become demarcated; at its cranial end is

blocks or *somites* [5]. Segmentation, which begins at what will become the occipital region of the head, is confined to the paraxial mesoderm. In the embryo shown in Fig. 22, p. 23, five somites have been formed; by the end of the 4th week, when the embryo has grown to a length of about 3 mm. (Fig. 23), the process has reached the first caudal or coccygeal segment, there being at this time 3 occipital and 30 body somites. Thereafter segmentation proceeds slowly in the caudal region, there being 8 or 10 caudal somites at the end of the 6th week, when the tail has reached its maximum development and the embryo is about 11 mm. long. Each segment carries certain potentialities—according to its position in the series. The first dorsal, for example, will give rise to one series of structures; the second to another series.

To understand the meaning of segmentation we must again appeal to comparative anatomy [6]. Segmentation marks the onset of vertebral characterization in the human embryo. In Fig. 50, *A*, a diagrammatic longitudinal section of a fish larva is reproduced to show the relations of the notochord; it and the neural tube, we have seen, are formed first in the head region and then grow backwards. In Fig. 50, *B*, another fish larva is depicted, with the notochord clothed with muscle segments or myotomes. A mere glance at such diagrams shows that the notochord or primitive vertebral column and the segmented spinal musculature represent a great sculling apparatus—the locomotory machine of the lowest and oldest vertebrates. Gill arches also appear in the human embryo very soon after segmentation has commenced (see Fig. 23), but even without their guidance one would infer, on the evidence of segmentation alone, that the human embryo in the 4th week is passing through a fish stage and that our vertebral column and spinal musculature represent a former locomotory system. The gill-segmentation is different and apparently older than the body-segmentation; and as we shall see, the gills are not fashioned out of the paraxial mesoderm.

NOTES AND REFERENCES

- [1] For literature on the subject
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Trans. Roy. Soc. Edin., 1937, 59, 165 (ferret); Asar, Y. H., *Jour. Anat.*, 1932, 66, 14 (rabbit).
- [2] West, C. M., *Contrib. Emb.*, 1930, 21, 25.
- [3] Streeter, G. L., *ibid.*, 1927, 19, 73.
- [4] For recent literature on the mapping of the blastoderm, see Pasteels, J., *Archiv. Biol.*, 1936, 48, 107 (reptilian); *ibid.*, 1936, 48, 381 (avian); Daleq and Pasteels, *ibid.*, 1936, 48, 609 (teleost); Vandebroek, G., *ibid.*, 1936, 47, 499

heart, blood-vessels, blood cells of all kinds and all forms of moving tissue cells. To this latter element of the mesoderm—the cells which form vessels, blood, connective tissue and mobile cells—is given the name of *mesenchyme*.

Notochord.—The notochord is the forerunner of the spinal column (Fig. 50, *A*). It is formed, as we have seen, by an ingrowth of ectoderm at the anterior end of the primitive streak. The plate of cells from which it is formed lies in the roof of the archenteron. Presently the chordal plate becomes folded off from the roof of the archenteron (Fig. 49) to form a rod of peculiar cells—the notochord. Only the anterior part of

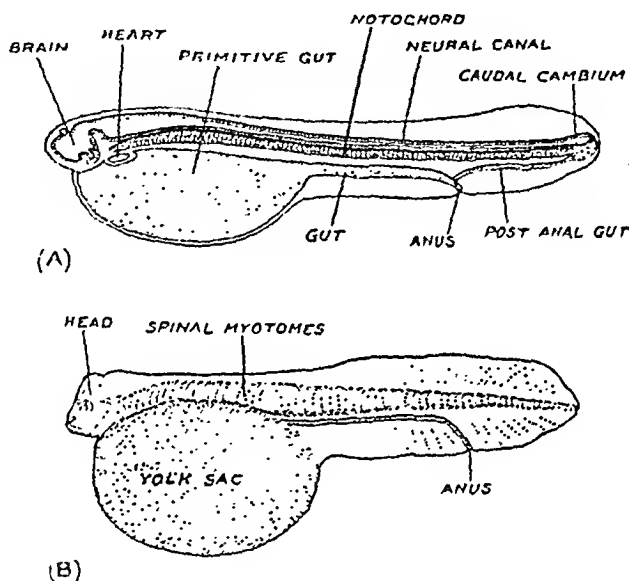


FIG. 50.

- A.* Diagrammatic longitudinal section of a larval *Polypterus*, a ganoid fish, to show the relations of the notochord. (After Graham Kerr.)
B. The larval form of *Lepidosteus*, another ganoid fish, to show the segmented vertebral musculature covering the notochord. (After Graham Kerr.)

the chordal plate is developed in the wall of the archenteron; the rest is formed above the roof of that cavity. It will thus be seen that the first representation of a skeleton is produced at an extremely early date, and that it appears as a support for the medullary plate when that plate is folded in to form a tube. Remnants of the notochord may persist within the vertebral axis and give rise to peculiar tumours.

Segmentation.—We have seen that the medullary folds begin to form early in the 4th week of development, when the embryonic plate is only about 1.5 mm. in length. Some days before they commence to fuse and thus enclose a tube, that part of the mesoderm which has been laid down by the side of the neural tube—the paraxial mesoderm (Fig. 49)—begins to be divided, from before backwards, into segmental

renal tubules if grown alone in a culture medium expands amorphously, but if mesodermal (connective tissue) cells are added to the culture, then tubules are formed [4]. This organizing power, although confined to embryonic life in vertebrates, is retained in the adult stage by certain invertebrates. Prof. Child found that when the head of a planarian worm was transplanted into the body of another, it caused that part of the host's body in which it was grafted to become a new body. The ova of certain insects developing on a living leaf or twig emit substances which bring about the formation of highly organized vegetable structures known as galls.

Dicbotomy and Twin Formation.—In the eighteenth century John Hunter discovered, as the result of varied experiments, that the apical bud of tree or stem exercises a restraining influence on buds placed lower on the stem. If the apical bud is destroyed and apical dominance thus lost, an adjacent bud assumes control and forms a new top. Or if the apical bud is merely damaged, then two centres of dominance may arise in its tissues, with the result that the apex divides and a double top is produced [5]. When the primitive streak appears on the embryonic plate of the human ovum the centre of dominance is at its anterior or cranial end. In the developing vertebrate ovum this centre is also the site of greatest metabolic activity [6]; there may be, as Julian Huxley supposes, a relationship between activity of metabolism and organizing potency [7], for if the metabolic activity at the anterior end of the primitive streak is greatly lessened, by submitting the developing ovum to radiations, to cold, to oxygen starvation or to solutions of noxious substances, then the organizing centre may be destroyed, with the result that no embryo is formed. Nevertheless chorion and amnion formation may still go on; the pregnancy thus produced is known as a "Mole" [8]. Or if the organizing centre is merely damaged then two centres of dominance may appear at the anterior end of the primitive streak with the result that a double embryonic area is produced. The embryos may be fused or conjoined in many different ways, giving rise to the various kinds of *double-monster* [9]. They may be joined head to head (craniopagus) or buttock to buttock (ischiopagus). Such monsters represent imperfect attempts to produce twins. In Fig. 52, *A*, two centres of development have appeared at the anterior end of the primitive streak, giving rise to two heads; the streak has remained single and hence there is but one body. In Fig. 52, *B*, the opposite has happened, giving rise to a monster with a single head and a double body. In Fig. 52, *C*, two embryogenic centres have been formed and two embryonic bodies, but the archenteron has remained single. Hence the developing body-walls of both embryos fuse; there is but one

graft, but from the tissues of the host. The "lip" graft played the part of "organizer." Previous experiments had prepared them for such a result. They had taken ectoderm which in the ordinary course of events would have become skin—that is, this area of ectoderm was *presumptive* epidermis—and grafted it amongst ectoderm destined to become part of the brain. The skin so transplanted became nerve tissue. They found that ectoderm destined to form a part of the spinal cord when transplanted into a skin region became skin. Let me illustrate this transformation. The United States of America receive immigrants from all parts of Europe and convert them into American citizens. At an early stage of development certain embryonic tissues have a similar power. None, however, have the organizing potency possessed by the dorsal lip of the blastopore.

The Power to induce Organization is Transferable.—If a fragment of presumptive epiderm is taken from the gastrula of a frog and placed within the pit at the anterior end of the primitive streak, it becomes endowed with the embryogenic powers of the dorsal lip. A material something of the nature of a growth-controlling hormone is transferred from the lip to the fragment. This observation seems to throw light on certain teratomatous tumours that may be formed in the human body along the track of the notochord. The latter structure, as we have seen, is produced from Hensen's node in the anterior lip of the primitive streak and may by accident retain and transfer the potency of the dorsal lip to adjacent tissues. The most common site for such tumours is the roof of the pharynx, near the anterior end of the notochord. An imperfect or tumour-like foetus projecting from the roof of the nasopharynx is known as an *epignath*. Teratomatous tumours also occur in the posterior mediastinum, the retroperitoneal tissues of the abdomen and in front of the sacrum and coccyx [2].

The Optic Cup as Organizer.—Although the dorsal lip of the blastopore is the crowning instance of embryogenic potency, yet the discovery that one developing tissue can exercise a controlling influence on a neighbouring tissue was made early in the present century by two men, Dr. W. H. Lewis of Johns Hopkins University and by Prof. H. Spemann of Freiburg [3]. They were making experiments on the optic cup which grows out from the embryonic fore-brain to form the retina. The ectoderm which overlies the cup grows inwards to produce the lens of the eye. They found that if the cup was excised no lens was formed, or if the developing optic cup is transplanted and placed under ordinary ectoderm, then the cup caused the overlying cells with which it came in contact to grow inwards and form a lens. The cup emits a growth-controlling (lens-producing) hormone. The epithelium of developing

renal tubules if grown alone in a culture medium expands amorphously, but if mesodermal (connective tissue) cells are added to the culture, then tubules are formed [4]. This organizing power, although confined to embryonic life in vertebrates, is retained in the adult stage by certain invertebrates. Prof. Child found that when the head of a planarian worm was transplanted into the body of another, it caused that part of the host's body in which it was grafted to become a new body. The ova of certain insects developing on a living leaf or twig emit substances which bring about the formation of highly organized vegetable structures known as galls.

Dichotomy and Twin Formation.—In the eighteenth century John Hunter discovered, as the result of varied experiments, that the apical bud of tree or stem exercises a restraining influence on buds placed lower on the stem. If the apical bud is destroyed and apical dominance thus lost, an adjacent bud assumes control and forms a new top. Or if the apical bud is merely damaged, then two centres of dominance may arise in its tissues, with the result that the apex divides and a double top is produced [5]. When the primitive streak appears on the embryonic plate of the human ovum the centre of dominance is at its anterior or cranial end. In the developing vertebrate ovum this centre is also the site of greatest metabolic activity [6]; there may be, as Julian Huxley supposes, a relationship between activity of metabolism and organizing potency [7], for if the metabolic activity at the anterior end of the primitive streak is greatly lessened, by submitting the developing ovum to radiations, to cold, to oxygen starvation or to solutions of noxious substances, then the organizing centre may be destroyed, with the result that no embryo is formed. Nevertheless chorion and amnion formation may still go on; the pregnancy thus produced is known as a "Mole" [8]. Or if the organizing centre is merely damaged then two centres of dominance may appear at the anterior end of the primitive streak with the result that a double embryonic area is produced. The embryos may be fused or conjoined in many different ways, giving rise to the various kinds of *double-monster* [9]. They may be joined head to head (craniopagus) or buttock to buttock (ischiopagus). Such monsters represent imperfect attempts to produce twins. In Fig. 52, *A*, two centres of development have appeared at the anterior end of the primitive streak, giving rise to two heads; the streak has remained single and hence there is but one body. In Fig. 52, *B*, the opposite has happened, giving rise to a monster with a single head and a double body. In Fig. 52, *C*, two embryogenic centres have been formed and two embryonic bodies, but the archenteron has remained single. Hence the developing body-walls of both embryos fuse; there is but one

umbilicus and one umbilical cord. Such monsters are conjoined belly to belly, as was the case in the Siamese twins [10]. In certain cases the

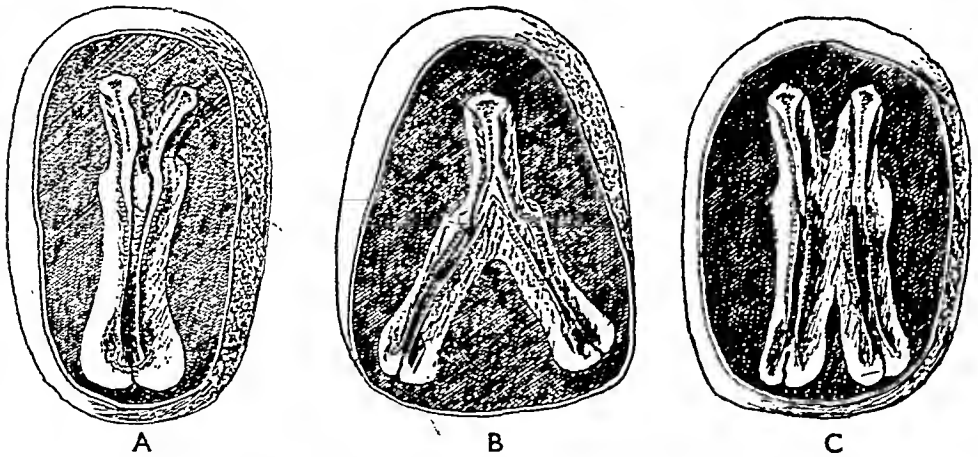


FIG. 52. Division of the Embryonic Plate, forming imperfect twins. A, anterior dichotomy; B, posterior dichotomy; C, intermediate union.

twin is represented by an amorphous foetus—with a non-functional heart (Acardiacus). In such cases a union has been effected between the umbilical arteries of the host twin and of the parasitic twin, with the

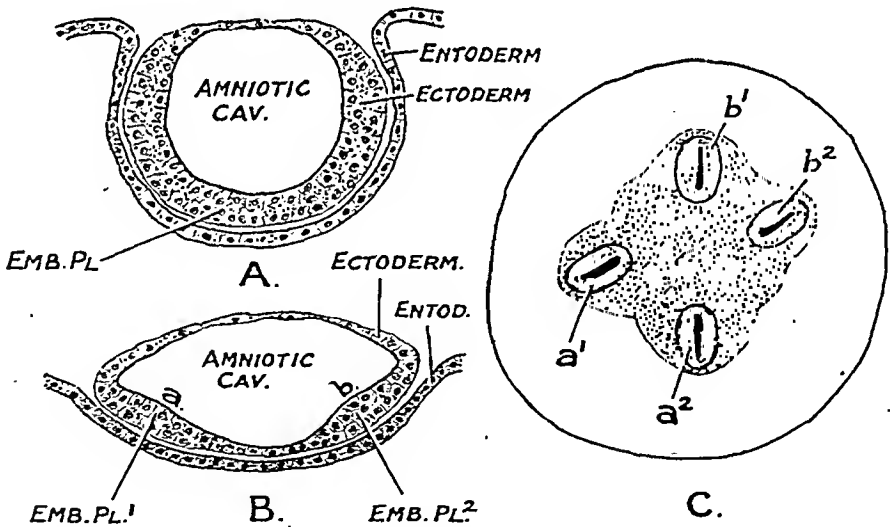


FIG. 53.

- A. First stage in the development of the embryonic plate of an Armadillo; the ectodermic plate is single.
- B. Second stage—the ectodermic plate now shows a separation into two embryonic plates, a, b.
- C. These plates, a, b, again subdivide, giving rise to four embryos, situated within a common amniotic cavity. All four are necessarily of the same sex. (After H. H. Newman.)

result that the latter comes to depend on the host for its circulation, which is reversed so that arteries carry blood towards the heart [11].

Monovular and Biovular Twins.—The embryogenic area at the anterior

end of the primitive streak may undergo dichotomy or division not as an abnormality due to the action of injurious conditions but as a natural or physiological process. In the gastrulate stage of the development of the Armadillo ovum, as Prof. H. H. Newman [12] discovered, not one but four centres of development arise (see Fig. 53). Four separate primitive streaks are produced, all within the same chorion, all four being of the same sex. Thus the young of Armadillos are born in hatches of four—"identical" quadruplets. In the same way two organizing centres may appear in the human embryonic plate, from each of which a primitive streak arises; two embryos are produced within the same set of membranes. The twins produced from a single ovum are necessarily of the same sex. They are "identical" twins [13]. On the other hand, two or more ova may be shed from the ovary at the same time; two or more may be fertilized; giving rise to twins or triplets, which may be male and female or of the same sex, as chance determines.

Imperfect or Intermediate Sex.—A subject akin to the one just discussed may be mentioned here. A male twin may have as its companion an imperfect male—one in which the gonadal glands produce neither spermatozoa nor ova; the internal and external sex organs are modelled on the female rather than on male lines. The imperfect male twin—the "free martin" of John Hunter [14]—is believed to have been originally of the female sex, but became altered in the following way. Such twins, although of biovular origin, are joined to a common placenta and a communication opens up in the placenta between the circulation of the stronger male twin and that of its weaker sister. In this way a hormone or sex controlling substance formed in the male foetus circulates in the body of the female twin, causing its sexual parts to assume a male configuration [15]. A fowl after laying fertile eggs may develop testicular tissue in her ovaries and assume the characters and behaviour of the cock. Although very rare, human beings do occur in whom both testicular and ovarian tissue are present in the same sex gland. Theoretically they are true *hermaphrodites*, but are never fertile.

If female embryos are subjected to repeated doses of male hormone (testosterone), their ovarian tissue atrophies and may be replaced by testicular tissue. Occasionally the gonadal tissue of male embryos when subjected to the female hormone (oestrone) undergoes atrophy [16]. If two larval forms of opposite sexes are so conjoined that their circulations communicate, then the ovary of the parabiotic twin undergoes atrophy but may become changed into a functional testis [17].

From such facts it is plain that sex is not irrevocably determined by chromosomes. A fertilized ovum, in spite of its genetic (chromosomal) constitution, may under certain conditions take on the structure and

appearance opposite to that of its true sex. An individual outwardly (phenotypically) a male may be constitutionally (genotypically) a female. Rarely we meet with persons in whom both ovary and testis are developed or in whom the sex glands combine both elements (ovario-testes); more frequently we meet with "neuters," in whom the glands are devoid of sex elements. There is in mankind a wide range of secondary sexual characters, ranging from the most robust of males to the most delicate of females.

Primordial ova of lower vertebrates may be influenced (determined)

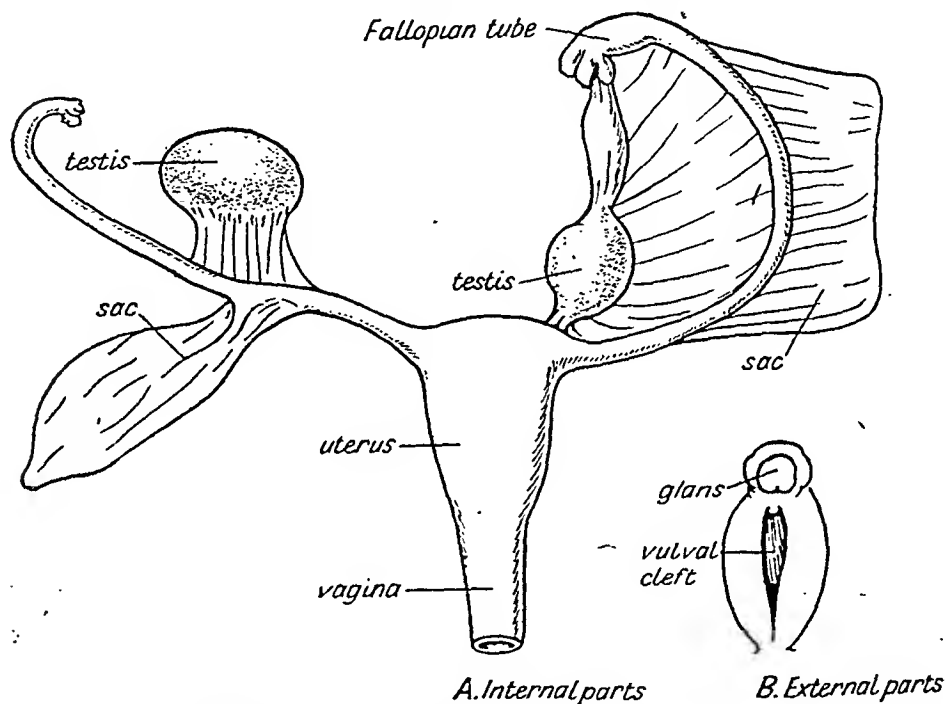


FIG. 54. Sexual organs of a child, aged 11 years, who, outwardly a female, was inwardly a male. (After Young.)

A. Internal parts: sac, gubernacular fold.

B. External parts.

by the region of the genital gland in which they come to be lodged, the cortical zone favouring a female manifestation, the medullary, a male. This power of regional differentiation appears to hold also for the developing sex glands of mammals [19]. Tumours of the cortex of the adrenal bodies have the power to produce a male hormone (androsterone); when such tumours occur in the bodies of young women, they lead to the development of secondary sexual characters of the male. Certain tumours which arise in the neighbourhood of the 3rd ventricle of the brain have a similar effect [20]. In spite of all these possible errors in sex differentiation, the vast majority of children are born unmistakable boys or girls.

Application of Cultural Methods to Embryology.—In 1907 Prof. Ross G. Harrison, of Yale, performed an experiment which opened up a vast new field of inquiry [21]. The great embryologist Wilhelm His of Leipzig had concluded from his studies of the spinal cord of human embryos that the anterior roots of spinal nerves were formed as outgrowths from the motor cells situated in the anterior horn. To put this inference to the test of experimental proof Harrison excised a fragment from the spinal cord of an early tadpole and kept the fragment alive in a drop of lymph suspended from a cover-glass. Placing the cover-glass under a microscope, he had the satisfaction of observing the outgrowth of processes from the cornual cells to form the nerve fibres of the anterior root. Thus began the practice of keeping fragments of developing and growing tissues alive in artificial media—the practice of “tissue culture.” By this method fragments of the embryonic heart and of other organs and tissues can be studied in their living state through many generations and their behaviour under varying conditions noted. In applying the methods of tissue culture to their subject, embryologists did but copy methods which bacteriologists had invented much earlier for the study of living micro-organisms [21].

By 1912 the late Prof. A. Brachet, of Brussels, had succeeded in keeping the blastoderm of the rabbit alive until the amnion was formed [22]. Since then the segmenting egg of many mammals, including that of man, has been kept alive until a morula mass has been formed. Many parts of the chick embryo have been excised and their development in artificial media noted. In 1926 Strangeways and Fell succeeded in keeping alive the part of the fore-brain which gives rise to the optic cup until a complete eye was formed. The membranes of the hatching egg offer a very good soil for the culture of embryonic grafts. Murray and Huxley grafted various parts of early limb buds on the chorio-allantoic membrane of the chick and found that each part produced the skeletal element proper to it. At a very early stage of development the parts of the future limb are already localized in the bud (see p. 593).

Transposition of Viscera.—Clinicians occasionally come across patients in whom the apex of the heart lies in the right side of the thorax. In such cases the great vessels are also transposed, the arch of the aorta crossing to the right, while the superior vena cava and right auricle are on the left. With transposition of the thoracic contents, it is usual for the contents of the abdomen to bear them company, liver, pylorus, duodenum and caecum being placed on the left side of the abdomen, while spleen and descending colon are on the right. Experimental embryologists have thrown a certain amount of light on this strange anomaly. Spemann excised the dorsal ectoderm of the developing

egg of a triton—the ectoderm which in due course would have been converted into brain and spinal cord. He replaced the excised piece, reversing it so that the caudal end occupied the situation of the cranial end. Nevertheless the brain developed in its normal situation—at the anterior end of the embryo—but the heart, vessels and abdominal contents were transposed. Further experiments led Spemann to suppose that the normal asymmetry in the arrangement of the contents of the thorax and abdomen was due to a dominance of the left half of the blastoderm over the right. If early dominance passed to the right half, then partial or complete transposition resulted [23]. A similar transference may occur between the right and left halves of the body. The majority of people are right-handed, dominance being in the right side; in left-handed people, who make up 2% of the total population, dominance is in the left half. As in transposition of the viscera, the transference of “handedness” may be partial or complete [24].

Duplication and Atrophy of Parts.—Parts of the body which arise as outgrowths, such as a digit, hand, foot, penis, nose, etc., may undergo duplication to a greater or lesser degree. In such cases we suppose that the group of cells which gives rise to such a part undergoes division or dichotomy, just as the growing-point of a stem may undergo branching. Transplanted limb-buds often divide; the regenerated tail of a newt is often double. We are dealing here with the same problem as in the production of twins; if the dominant centre of growth loses control, as a result of being subjected to injurious conditions, then it may be replaced by two separate centres. If the injury is so great that the growing centre is killed or starved then the part fails to develop. The limbs may be represented by fleshy papules; certain parts of hand and forearm, foot and leg may be absent; the external nose or the lower jaw may remain a mere rudiment. The immediate cause of such growth-failures in human embryos has not been discovered, but light is thrown on some of them in the paragraphs which follow.

In Fig. 55 are depicted two congenital malformations of the face; *A* shows the condition known as *Cyclops*, where the eyes are fused to a greater or less degree in the midline of the face; in *B* another kind of malformation is represented, one in which there is a failure in the development of the lower parts of the face, especially of the upper and lower jaw or mandible. The failure may be slight or so severe as in Fig. 55, *B*, where the mandibular arch may be said to be absent. When the suppression of parts is as complete as in Fig. 55, *B*, where the right and left external ears fuse where a chin ought to be, the condition is known as *Otocephaly*.

Experimental embryology is throwing light on those obscure but not

uncommon malformations of the face. Experiments have proved that the cells which give rise to the cartilage of the mandibular arch (Meckel's cartilage) and to the traheculae and palato-quadrate cartilages of the base of the skull are developed in the margin or crest of that part of the medullary plate which gives rise to the fore-brain. At an early stage of development these cartilage-forming cells migrate from the margins of the fore-brain plate to take up their facial stations. If, then, the developing margin of the fore-brain is exposed to noxious conditions, such as X-ray or other forms of radiation, to chemical substances, or to unusual degrees of temperature, the cartilage-forming cells are arrested in their migration or perish, with the result that facial development is

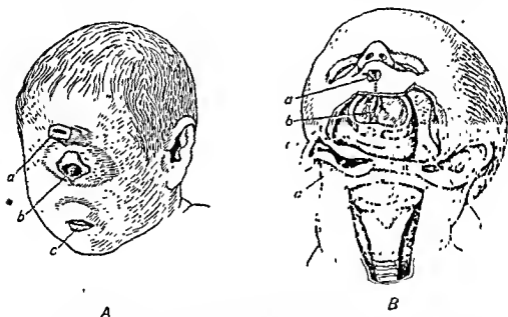


FIG. 55

- A. Face of a fulltime child, showing the condition known as Cyclops. *a*, Single tubular nose; *b*, fused eyes; *c*, reduced mouth
 B. Face of a fulltime child showing the condition known as Agnathia. *a*, Lips and mouth; *b*, buccal cavity; *c*, fibrous representative of the mandibular arch; *d*, right external ear and meatus; *e*, rudiment of jugal arch.

arrested. The earlier the stage of development at which the noxious agent is applied and the more severe the application, then the greater is the degree of facial deformation. In Cyclops the incidence of damage falls on the anterior growing margin of the fore-brain plate [25].

Intrauterine Amputations and Amniotic Adhesions.—A monograph published by Dr. G. L. Streeter [26] throws a new light on the nature of certain pathological bands of connective tissue—passing from the foetus to the amnion and known as *amniotic adhesions*—and also upon the manner in which limbs are “amputated” within the uterus. An example of an amniotic band is shown in Fig. 56; it hinds an unenclosed

mass of cerebral tissue on the head to the inner membrane (amnion) on the placenta. To understand the nature of this band it is best to consider first the "amputation" of foetal limbs. In Fig. 57 are reproduced, from Dr. Streeter's drawings, sections of the right and left hand of a 7th-month foetus in which several digits have been lost by "amputation"

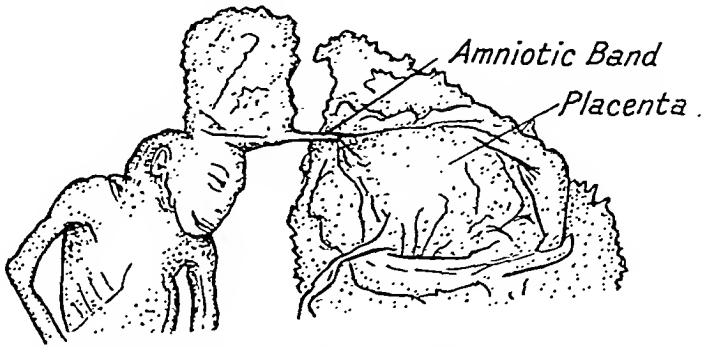


FIG. 56. An Anencephalic Foetus with an amniotic band binding a cerebral excrescence to the placenta. (Streeter.)

and in which surviving digits are bound by bands of the same nature as amniotic adhesions. Clearly the condition seen in these two foetal hands has many close resemblances to the necrosis which follows a circulatory failure in the hands of adults—as a result of frostbite or occlusion of the main arteries of the arm. It seems highly probable

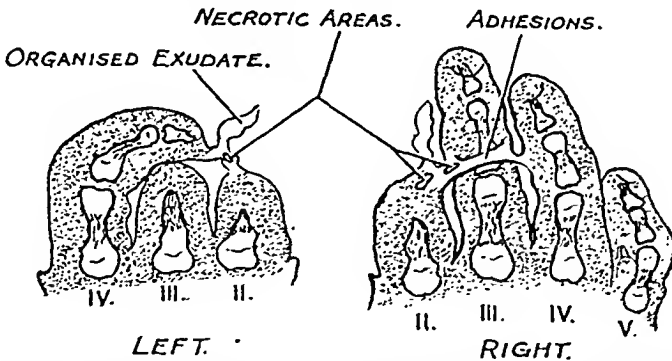


FIG. 57. Sections of the digits of the right and left hands of a 7th-month foetus in which digits have been "amputated" and adhesive bands formed. (Streeter.)

that such intrauterine amputations, amniotic bands and adhesions may be the result of circulatory failure in the foetal tissues—due to a breakdown in the placental circulation. The effects of circulatory failure in the embryo and foetus differ from those which are seen in the adult for two reasons: (i) the foetus is surrounded by a warm cultural medium—the amniotic fluid; (ii) the foetal tissues withstand lack of oxygen and of nourishment much better than adult tissues. When the circulation is cut off from an adult hand it dies and presently a ring forms

at the junction of dead and living tissue—a ring at which the living tissue throws off or “amputates” the dead. When the circulation fails in a foetal limb a ring of amputation is formed, but as the lymph exudes at this ring it is invaded and organized by fibro-blasts. In this way constricting rings of fibrous tissue are formed at sites of amputation. The part beyond the constricting ring may drop off and amputation is thus completed. More frequently part of the limb distal to the constricting band survives, as in the hands shown in Fig. 57. Not only the limb-buds but all actively growing tissues may be the sites of foetal necrosis. For example, circulatory failure may occur when the medullary folds which are to form the brain and its coverings are in process of union, resulting in the outpouring of organized lymph and the formation of such a band as is shown in Fig. 56. Many congenital linear scars of the face and of the head are manifestations of this plastic disorder of early foetal life, which may be named *dysplasia foetalis* [27]. Tags of skin are often formed along the site of facial scars.

More remarkable still is the fact that this foetal disorder can be produced in rats and mice by experimental means and that a certain proportion of the progeny of such animals will inherit the disorder.

Injury to the Germplasm.—In 1924 Bagg and Little [28] instituted experiments which throw light on the hereditary nature of some malformations of the human body. They submitted the ovaries of mice to doses of X-rays; such mice produced progeny amongst which many suffered from malformations—club foot, polydactyly, etc. These deformed mice, although they themselves had not been submitted to X-rays, produced a high proportion of malformed young, showing that the chromosomes of the germ cells can hand on changes originally produced in them by artificial means.

Knowledge relating to deformed and monstrous fetuses is known as *Teratology*. Mention will be made of the commoner developmental malformations as we deal with the regions of the body in which they occur.

NOTES AND REFERENCES

[1] As regards the subject-matter of Chapter IV, two changes must be noted since the appearance of the last edition. The first of these is the death of Prof. Hans Spemann; he died on September 27, 1941, aet. 72, regretted by embryologists in every part of the world. The second matter which requires note is the rapid expansion of the field of experimental embryology: it has grown far beyond the scope of a single chapter. Hence my readers in search of recent literature and discovery must consult such works as *Embryonic Development and Induction*, by Spemann (Oxford, 1938); *The Elements of Experimental Embryology*, by Huxley and De Beer, 1934; and, above all, *Biochemistry and Morphogenesis*, by Joseph Needham, 1942.

[2] For recent accounts of teratomatous tumours, see: Nicholson, G. W., *Guy's*
3*

CHAPTER V

AGE CHANGES IN THE EMBRYO AND FOETUS

In Chapter I, having followed the developmental changes in the human embryo during the first 5 weeks, when it had reached a crown-rump length of 5 mm. ($1/5$ in.) and the condition of parts shown in Fig. 58, we had to break away in Chapters II, III and IV to note the manner in which it effected a lodgment in the uterus and to examine certain processes which give rise to fundamental parts of the embryonic body. In this chapter we return to trace the further history of the embryo, to watch it becoming transformed into a foetus and to register the subsequent changes during the 9 months it spends in its mother's womb.

In recent years our knowledge concerning the rate at which the human

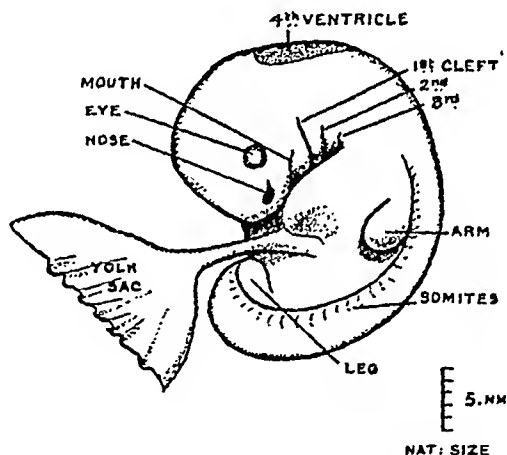


FIG. 58. Outline of a Human Embryo 5 mm. in length and in the 5th week of development. (Magnific. 5 diams.) (Reconstructed by Prof. Keibel and Dr. Elze.)

embryo grows and the stages through which it passes week by week has become more accurate. The late Prof. Mall collected facts relating to all cases where the age of an embryo had been ascertained and by tabulating his data was able to estimate the size and stage of development reached by an average human embryo week after week [1]. His main results, so far as concern the first 2 months, are set out in Fig. 59, taken from an article written by his distinguished pupil, Prof. Herbert Evans. Six stages of development are represented: at the end of the 3rd, 4th, 5th, 6th, 7th and 8th weeks. Under each embryo is given the mean length it should reach at a certain date, but it has to be remembered that the

rate of growth varies in embryos and foetuses just as in children, and that some will be precocious while others will be backward. The measurements relate to fresh specimens, for when embryos are preserved and prepared for microscopic examination they shrink in size. It is convenient to regard 3 mm. as measured from the crown to the rump of the embryo as marking the end of the 4th week, and 5 mm. as an index of the end of the 5th week of development. In the 6th, 7th and 8th weeks the embryo adds almost one millimetre to its length daily, being about 25 mm. (1 in.) at the end of the 8th week. Hence we may

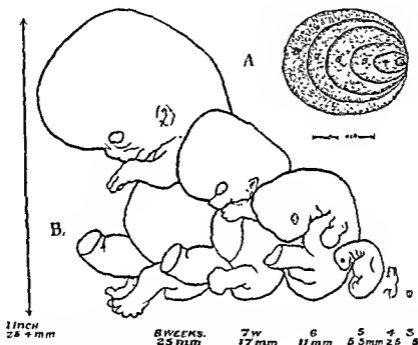


FIG. 59. Series of six drawings illustrating the stages of growth from the end of the 3rd week to the end of the 8th. In a corner of the figure is a diagram to illustrate the rate of growth of the chorionic vesicle at corresponding dates (Prof. H. M. Evans)

readily estimate the age of an embryo or foetus under 25 mm. in length by regarding the first 5 mm. as representing 35 days' growth and adding a day for every additional millimetre of its length. For example, the age in days of an embryo measuring 15 mm. in length would be estimated thus: 5 mm. = 35 days + 10 for the additional 10 mm. = 45 days. In the 9th, 10th, 11th, 12th, 13th and 14th weeks—up to the end of the 3rd month—when the crown-rump length amounts to 100 mm. (4 in.)—the daily rate of growth is approximately 1.5 mm. From the end of the 5th month the crown-rump length of a foetus stated in millimetres is an approximate expression of its age in days (Jordan).

External Changes in the 6th week.—As may be seen by comparing

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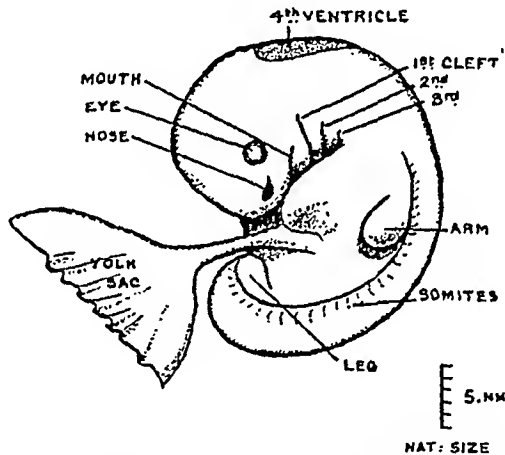


FIG. 58. Outline of a Human Embryo 5 mm. in length and in the 5th week of development. (Magnific. 5 diams.) (Reconstructed by Prof. Keibel and Dr. Elze.)

embryo grows and the stages through which it passes week by week has become more accurate. The late Prof. Mall collected facts relating to all cases where the age of an embryo had been ascertained and by tabulating his data was able to estimate the size and stage of development reached by an average human embryo week after week [1]. His main results, so far as concern the first 2 months, are set out in Fig. 59, taken from an article written by his distinguished pupil, Prof. Herbert Evans. Six stages of development are represented: at the end of the 3rd, 4th, 5th, 6th, 7th and 8th weeks. Under each embryo is given the mean length it should reach at a certain date, but it has to be remembered that the

leg, and a plate-like hand and foot. In point of differentiation the fore-limb is always in advance of the hind. At the close of the 6th week the first appearance of webbed digits can be detected, and at the same time, when the length of the embryo is about 11 mm., the tail reaches its maximum development (Fig. 60); in the 7th week retrogression has already set in. The umbilical cord becomes lengthened and more clearly differentiated in the 6th week; between the attachment of the cord to the ventral wall of the embryo and the gill-formation of the primitive pharynx is seen the bulging eminence of the heart (Fig. 58); below the heart eminence, as may be seen in Fig. 60, there appears in the 6th week a second eminence, that caused by the developing liver.

At the beginning of the 6th week cartilage is being formed; towards

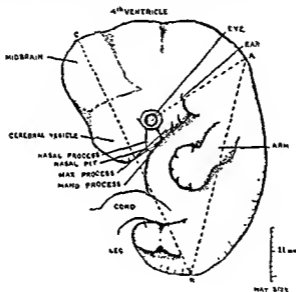


FIG. 61. Outline of the 6th week embryo.

the end of that week centres of ossification make their appearance. Although the spasmodic motions of the foetus, known as "quickening," do not occur until the 5th month, even in a foetus of the 6th week certain unregulated movements can be elicited [3].

Embryo-Foetus.—During the 7th week the embryo becomes a foetus—the transformation being well shown in Fig. 59. In its crown-rump length the embryo expands from 11 to 17 mm., but the characteristic changes are seen in the face, head and limbs. An early stage of the 7th week is shown in Fig. 61; the basal parts of the face are being laid down. Under the eye are seen the nasal processes carrying the open nasal cavities backwards into the region of the mouth, while growing forwards

Figs. 58 and 60, the 6th week constitutes a period of rapid transformation. Not only does the length of the embryo increase from 5 mm. to 11 mm. but there are very definite changes in the form of its external parts. At the end of the 5th week the gill-arch system of the primitive pharynx is at its height, four arches being distinguishable ; in the 6th week the 3rd and 4th arches sink into a pit in the neck—the *cervical sinus*—(Fig. 60), while the 2nd or hyoid arch grows backwards over the pit and thus hides the hinder arches [2]. Here we are witnessing the closing in or operculation of the branchial arches—as it takes place in gill-bearing vertebrates.

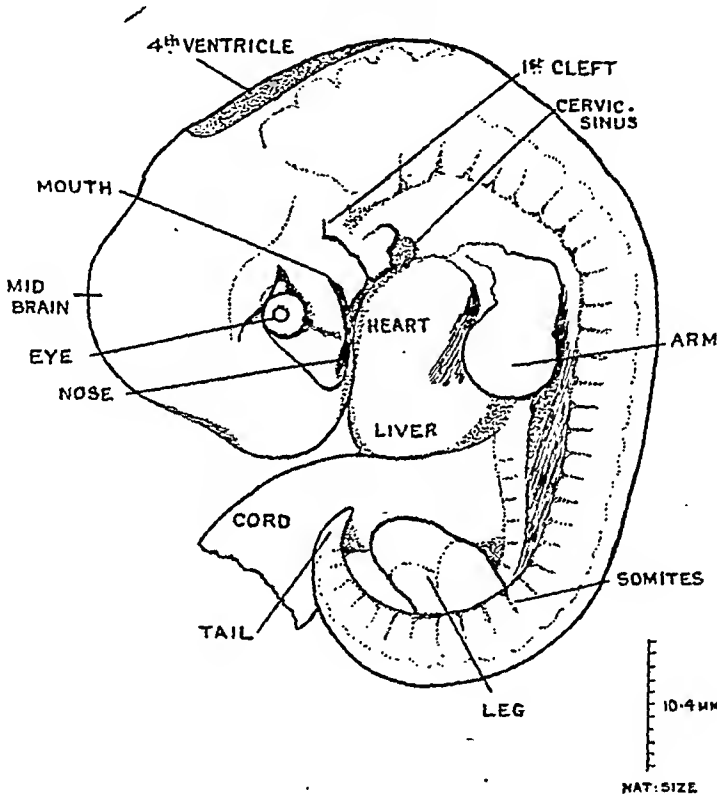


FIG. 60. Outline of a Human Embryo 10.4 mm. long and in the 6th week of development. (Magnific. 5 diams.) (After Broman.)

Even at the close of the 6th week the face is represented merely by a forehead filled out by the relatively small fore-brain vesicle ; behind and under the forehead are seen the nasal, maxillary and mandibular processes which will give rise to the face proper. All of these elements have made headway during the 6th week (Figs. 58, 59, 60). The head region even in the 6th week is still tubular in form ; the mid and hind brains form the greater part of the central nervous system, for the cerebral vesicles have as yet only begun to grow out from the fore brain. The limb-buds, which in the 5th week were still undemarcated into segments, now show their three primitive parts—upper arm and thigh, forearm and

if by a month we mean 30 days—270 days in all—we are as near the truth as our present evidence will take us [4]. Medical men can seldom discover the exact date of conception and hence to get a fixed point for a reckoning they begin their estimate counting from the 1st day of the mother's last menstrual period, and taking this day as a fixed point, count that parturition will take place 280 days hence. The most common time for ovulation to occur is the 15th day of the sexual cycle, taking the 1st day of menstruation as marking the beginning of the cycle. If we accept the 15th day as that of conception as well as of ovulation,

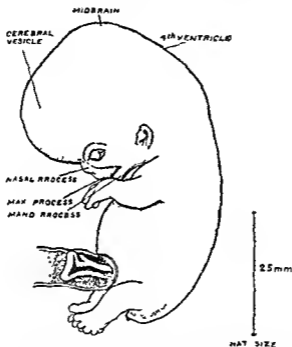


FIG. 62. Outline of a Foetus 22 mm. long, and at the end of the 2nd month of development. (After Broman.)

then we must deduct the preceding 14 days from 280 to find the period of gestation. The period of gestation is thus 266 days. The 266th day is the hull's-eye at which Nature aims, but even the best of marksmen make "inners" and "outers," and it is so in all of Nature's shootings. She is ever subject to the law of chance; hence in all developmental and growth manifestation we meet with variation round a mean.

By the 266th day the foetus has attained a weight of about 7 lb. and a height, if we measure from crown to rump (sitting height), of 336 mm., but if we include the lower extremities (standing height) the measurement is 500 mm. (nearly 20 in.). Ossific centres have appeared in the distal end of the femur and proximal end of the tibia. Usually, too, centres have appeared in the head of the femur and in the head of the

beneath the eye are to be observed the maxillary processes which will provide the bases of the upper jaw. Still further back in the pharynx (Fig. 61) are seen two comparatively small processes—the mandibular (1st arch) and hyoid (2nd arch). Behind the hyoid arch there is a depression marking the cervical sinus. By the end of the 7th week the nasal, maxillary and mandibular processes have united to form a relatively small face; at the upper end of the postmandibular cleft has appeared the rudiment of an ear. The changes in the head itself are also apparent; at the end of the 7th week the cylindrical cranial form is being replaced by one more distinctly globular; the forehead in particular has become enlarged. These changes are due to the rapid expansion of the cerebral vesicles during the 7th week. The changes in the limbs are also very evident; they are now folded on the belly-wall, palm towards palm and sole towards sole; the digits are demarcated. The tail is disappearing. The head is no longer bent forwards with the forehead touching the root of the umbilical cord, but is lifted up, for the embryonic flexure of the cervical region is being undone and a narrowing of the post-cranial region to form a neck becomes apparent. The heart is now completely divided into right and left chambers and the growth of the neck is lifting the pharyngeal region away from the heart. With these changes in the facial region, in the head, neck, limbs and heart the embryo of the 6th week becomes the foetus of the 7th. One other very important event also characterizes this stage of transformation: the *cellular blastema of the skeleton* is now changing rapidly into cartilage and into bone. It also becomes possible to distinguish the ovary from the testicle.

Changes in the 8th week.—At the end of the 8th week the crown-rump diameter measures about 25 mm. (1 in.). The changes of this week are a continuation of those we have just described (Fig. 62); the nasal and maxillary processes have fused to form the upper face; the upper lip is completed, but the palatal processes have not yet separated the buccal from the nasal cavities. The cerebral vesicles are expanding rapidly backwards; the neck is being differentiated and the limbs are making progress. The rudiment of the external genital organs is apparent, but as yet gives no clue to sex. The intestinal loop lies within the root of the umbilical cord. The intestinal loop will be withdrawn about the 10th week; in the same period movements appear in the limbs. Henceforward, until the end of gestation, the chief changes are those of growth.

The Full-Time Foetus.—We speak of the period of human *gestation*—the time spent by the human young in the uterus of the mother, preparatory to an independent existence—

after the menarche or catamenia in women and after puberty in the male. There is a period of growth (12-14 years) when girls are taller than boys of the same age. In the body of adults the length of the upper extremity is, in the mean, 88% of the length of the lower; there is a stage in foetal development when the upper extremity is the longer, being 125% of the lower (Devonport). Growth—the production of new tissue—in lung, liver, kidney, spleen, stomach and bowels—goes on throughout adolescence, but much has yet to be discovered before we can say when our various organs reach maturity. The human brain attains its greatest weight in the 19th year [8].

Childhood and Adolescence.—In recent years measurements have been made of the growth of the body in childhood and in adolescence of peoples in all parts of the world. In some instances the same groups have been measured and recorded year after year, from infancy to adolescence. Such examinations have revealed that each child has its own rate and rhythm of growth and that the results obtained from measurements of large groups can be expressed only by statistical methods. These measurements have proved that there has been a continuous increase of stature in the peoples of Europe and North America during the past seventy years [9].

Table of Growth.—It is impossible for anyone to remember the dimensions reached during the various stages of foetal development and growth, but it is often convenient to have a table of measurements for reference. The one given here was prepared by the late Prof. Mall [1]:

CROWN-RUMP LENGTH.	STANDING HEIGHT.	AGE IN WEEKS.	AGE IN DAYS.
1.0 mm.	—	3	21
2.5 "	—	4	28
5.5 "	—	5	35
11 "	—	6	42
17 "	—	7	49
25 "	—	8	56
32 "	—	9	63
43 "	—	10	70
53 "	—	11	77
68 "	—	12	84
81 "	—	13	91
100 "	149	14	98 end of 3rd month.
111 "	—	15	105
121 "	—	16	112
134 "	—	17	119
145 "	223	18	126 end of 4th month.

humerus [5]. It sometimes happens that birth takes place at the end of the 7th month, when the foetus weighs between 4-5 lb. and in its standing height measures 400 mm. or less, its sitting height being then about 265 mm. In such premature children, who have always a defective heat-regulating mechanism, it will be observed that the tips of the nails just reach the ends of the nail beds, whereas in the full-time child the nail edges are free and projecting. The full-time child has also an out-crop of hair on the head; lanugo—foetal hair—can be detected on various parts of the body. The hair tips which break on the surface of the skin about the end of the 4th month may be plentiful on the scalp at the end of the 7th, but the skin is then of bright lobster-red, the subcutaneous tissue is less stored with fat and the sebaceous covering, known as the *vernix caseosa*, forms a thin and unequal coating [6].

Comparative Rates of Development and Growth.—It is of interest to note how man stands to other animals in rate of development and of growth. The period of gestation in the mouse is 21 days; its young are born nude and blind. In the guinea-pig the period is nearly three times as long—62 days; its young are born fully furred, with senses and limbs well developed. The newly born guinea-pig has reached a stage of ossification equal to that of a child eight years of age. The mean period of gestation in the rhesus monkey is 164 days; its milk teeth are cutting at birth; maturity is reached in the 7th year. In anthropoid apes, taking the chimpanzee as an example, the mean period of gestation is 236 days, 30 less than in man. The infant chimpanzee, at the end of its first year, although it weighs only 3 lb. at birth, has reached a stage of ossification corresponding to that of a human child between two and three years of age. Growing at about the same rate as a human child until the 8th year, its body suddenly rushes toward maturity, which it attains about the 11th year. The male chimpanzee then weighs about the same as an average man. In the evolution of the human body all three periods—foetal, infantile and adolescent—have been prolonged, especially that of adolescence [7] (Wingate Todd).

Heterochrony.—We have been discussing the different rates at which the bodies of man and ape mature. When we look into the development and growth of the parts and of the tissues of the body we find that they too manifest heterochrony, i.e. varying rates in reaching maturity. The eye and the internal ear have done most of their growth by the end of the 2nd year; in a foetus of the 8th week the head is equal to 45% of the weight of the body. By the end of the 6th year the human brain has reached 90% of its final size. The lymphatic system reaches its greatest relative growth in childhood, while the sexual system is latent until puberty (14-16 years). The secondary sexual characters develop

[4] Eden, T. Watts, *Lancet*, 1923, 1, 1199; Asdell, S. A., *Jour. Amer. Med. Ass.*, 1927, 89, 509. See also references under note [7].

[5] References to the literature dealing with dates at which centres of ossification appear are given on p. 647, note [18].

[6] Scammon and Calkins, *The Development and Growth of the External Dimensions of the Human Body*, 1929; Scammon, R. E., *Anat. Rec.*, 1937, 68, 222 (nomographs of foetus and child); Waheed, A., *Zeitsch. Anat. u. Entwickl.*, 1937, 106, 558 (anatomy of thoracic organs at birth).

[7] For literature on life-periods of man and of ape, see Hartman, C. G., *Contrib. Emb.*, 1932, 23, i (of rhesus monkey); Zuckerman and Parkes, *Proc. Zool. Soc. Lond.*, 1932, p. 140 (baboons); Elder and Yerkes, *Proc. Roy. Soc.*, 1936, 120 (B), 409 (chimpanzee); Schultz, A. H., *Contrib. Emb.*, 1937, 27, 717 (for periods in monkeys, apes and men); Todd, T. W., *Amer. Jour. Dis. Child.*, 1932, 43, 533; Brandes, G., *Zool. Gart.*, 1931, 43, 39 (growth of anthropoid apes).

[8] Lucas Keene and Hewer, *Lancet*, 1923, 1, 1054 (maturation of tissues); Davenport, C. B., *Proc. Nat. Acad. Sc.*, 1934, 20, 359 (growth in proportions of limbs);

[9] (rates of growth
f growth in tissues

and organs); for literature on heterochrony, see references to works by Huxley and De Beer, and by Needham, Chapter IV, note [1].

[9] Fleming, R. M., *Med. Resear. Coun. Spec. Rep.*, 1933, No. 190; Todd, T. W., *Atlas of Skeletal Maturation*, 1937; Blackfan, K. B., *Growth and Development of the Child*, 1933; Meredith, H. V., *The Rhythm of Physical Growth*, 1935; *Handbuch der Anatomie des Kindes*, edited by Karl Peter, 1936; *Growth and Development of the Child* (White House Conference, 1933); Harris, H. A., *Memorandum to Committee on Infant Schools* (H.M. Stationery Office, 1933); Simmons and Todd, *Growth*, 1938, 2, 93 (dentition and growth).

CROWN-RUMP LENGTH.	STANDING HEIGHT.	AGE IN WEEKS.	AGE IN DAYS.	
157 mm.	—	19	133	
167 "	—	20	140	
180 "	—	21	147	
192 "	295	22	154	end of 5th month.
202 "	—	23	161	
210 "	—	24	168	
220 "	—	25	175	
230 "	331	26	182	end of 6th month.
237 "	—	27	189	
245 "	—	28	196	
252 "	—	29	203	
265 "	400	30	210	end of 7th month.
276 "	—	31	217	
284 "	—	32	224	
293 "	—	33	231	
301 "	443	34	238	end of 8th month.
310 "	—	35	245	
316 "	—	36	252	
325 "	—	37	259	
336 "	500	—	270	end of 9th month.

NOTES AND REFERENCES

[1] I have retained Prof. Franklin Mall's table of dates and measurements originally published in the *American Journal of Anatomy* (1918, 23, 397). Dr. George L. Streeter, who succeeded Prof. Mall as Director of the Department of Embryology of the Carnegie Institution in 1917, is preparing (1945) a new table based on a greater assemblage of data than was available to his predecessor. In preparing his new table Dr. Streeter rightly insists that the best guide to the age of an embryo is not its size but its degree or stage of development. He has already published (*Contrib. Emb.*, 1942, 30, 213) accounts of two stages, Stage XI, Embryos with 13-20 somites (23-25 days); Stage XII, Embryos with 21-29 somites (26-27 days); his length measurements are slightly greater than those given by Prof. Mall.

The stages distinguished by Dr. Streeter are the following: I, Ovum; II, Segmenting ovum; III, Free Blastocyst; IV, Implanting Blastocyst; V, Implanted, non-villous Blastocyst; VI, Primary villi appearing; VII, Germ-disc formed, villi branching; VIII, Primitive node and streak appear; IX, Neural folds and notochord appear; X, Early somites, 1-13; Stages XI, XII, as above; XIII, All somites formed (28 days, length 4-5 mm.); XIV, Lens vesicle has appeared, length, 5.5-8 mm., age 29 days.

[2] For Prof. J. E. Frazer's interpretation of cervical changes, see Chapter XVIII, p. 349.

[3] Coghill, G. E., *Archiv. Neur. Psych.*, 1929, 21, 989; Windle and Fitzgerald, *Jour. Compar. Neur.*, 1937, 119, 493; Snyder and Rosenfeld, *Amer. Jour. Physiol.*, 1937, 119, 153 (prenatal respiratory movements); Barcroft, Sir J., *Jour. Physiol.*, 1936, 87, 73 (foetal movements in sheep); Harris, H. A., *Jour. Anat.*, 1937, 71, 516; Barcroft, Sir J., *Researches on Pre-Natal Life*, 1947.

spinal column of man, although similar to that of the anthropoids, shows many peculiar adaptations to his manner of locomotion. These adaptations become especially manifest as the child learns to walk [1], and are best realized by a survey of the pyramids and curves of the spine.

Pyramids of the Spine.—The spine, when viewed from the front, is seen to be made up of four pyramids: (i) Cervical; (ii) upper dorsal; (iii) dorso-lumbar; (iv) sacrococeygeal (Fig. 63). The bases of the two upper pyramids meet at the disc between the 7th cervical and 1st dorsal vertebrae; the bases of the lower two at the disc between the 5th lumbar and 1st sacral vertebrae. The apices of the two middle pyramids meet at the disc between the 4th and 5th dorsal vertebrae, which have therefore the narrowest bodies of the vertebral series. The narrowing in the upper dorsal region is due to the fact that the weight of the upper half of the trunk is partly borne by, and transmitted to the lower dorsal region, by the sternum and ribs, which thus relieve the spine to some extent (Fig. 63). At the sacrum the weight is transferred to the pelvis and lower limbs, hence the rapid diminution of the sacrum and coccyx. A well-marked thickening or bar in each ilium runs from the auricular surface to the acetabulum along the pelvic brim and transmits the weight to the femora.

Curves of the Spinal Column.—There is only one curve—an anterior concavity—until the 3rd month of foetal life (Fig. 64, A). About the beginning of the 4th month the sacro-vertebral angle forms between the lumbar and sacral regions (Fig. 64, B). Soon after birth the cervical and sacral curves have appeared, but the sacral not to a pronounced extent (Fig. 64, C). The lumbar curve appears as the child learns to walk. It is produced to allow the body to be brought vertically over the lower extremities. The sacral and cervical curves also become at that time more marked (Fig. 64, D). The dorsal curvature, the flexible cervical bend and the sacro-vertebral angle are primary curves and are present in all mammals. The others are

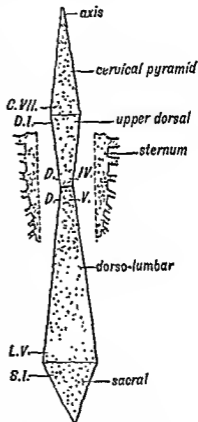


FIG 63. Diagram of the Pyramids of the Spine.

CHAPTER VI

THE SPINAL COLUMN AND BACK

Stages in the Development of the Spinal Column.—In previous chapters the main facts relating to the development of the human body during the 1st and 2nd months have been briefly sketched. We now turn to the consideration of particular parts of the human body, and naturally take up first the vertebral column—the main axis of the body. The most primitive form of axial support, the notochord, begins to appear in the human embryo during the latter part of the 3rd week and is completed by the end of the 5th. In amphioxus the notochord forms a permanent structure; in all vertebrate animals it is replaced by a segmented or vertebral axis. In the evolution of the spinal column three stages are recognized: (i) one in which the skeletal segments are composed of cellular or mesenchymatous tissue; (ii) a cartilaginous stage, in which the cells of the mesenchyme (see p. 60) become modified into cartilage-forming or chondrogenous cells; (iii) a final stage where the cartilage is replaced by bone. In the human embryo we see these three stages appear in succession; at the beginning of the 2nd month the membranous foundation of the vertebra is being laid down; in the middle of that month the cartilaginous change has commenced; by the beginning of the 3rd month ossification has set in. In only certain groups of fishes is the cartilaginous stage a permanent one.

Stages in the Evolution of the Human Spinal Column.—We have already seen that the vertebral column and its muscles appear first as a great flexible scull for driving the animal forward (p. 60), but in nearly all mammals the vertebral column comes to serve as a horizontal axis or arch, which is supported on the fore and hind limbs. In a small group, however, which includes the anthropoid apes and man, the spinal column no longer forms a horizontal but a vertical axis or column. These higher primates are upright or *orthograde* when they move, in contradistinction to the ordinary four-footed mammals, which are *pronograde*. There is no doubt that the orthograde posture was evolved from the pronograde. Although the anthropoid apes are orthograde, yet they use their arms in locomotion, to assist their lower extremities in supporting the weight of their bodies. Man is also orthograde, but he differs from the anthropoids in supporting the weight of his body entirely on his lower extremities. Hence we find that the

established by selection. Such vertebral variations are frequent, and are often of clinical importance.

I. The sacro-lumbor.—The 25th vertebra in 95% of people forms the 1st sacral; in 1% the 24th, and 3% the 26th. These percentages are drawn from the observations of Paterson, Rosenberg, Willis, Brailsford and others who have made researches on this subject [5]. The vertebral formula is not fixed. Rosenberg's investigations showed (Fig. 65) that it is the 26th vertebra that forms the first of the sacral series in the early embryo; later the 25th throws out great lateral masses, and thus forms a connection with the ilia. Bardeen could not confirm Rosenberg's observations; he found that the vertebra which was to form the first sacral—whether it was the 24th, 25th or 26th in the vertebral series—

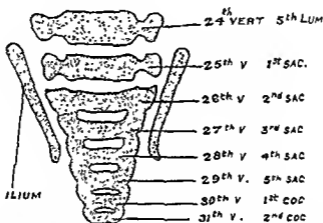


FIG. 65. A section of the lumbo-sacral region of the spine in a Foetus at the end of the 2nd month, showing the 26th vertebra forming the 1st sacral. (After Rosenberg)

took on a predominance at its earliest appearance. In the lower primates (monkeys) the 27th forms the 1st sacral; with the evolution of man the 26th, then the 25th underwent sacral modifications, the trunk being correspondingly shortened [6]. The lumbar region of the human spine grows much more rapidly after birth than either the cervical or dorsal region, in order to form an elongated flexible pillar for the support of the upper part of the body. In anthropoid apes the lumbar region is relatively short, as in the child at birth. It will be seen that the number of lumbar vertebrae in man is not definitely fixed. The anterior point of attachment of the ilium fluctuates from the 24th to the 26th vertebra. With the sacral transformation of the 25th and 26th (lumbar) vertebrae, there is usually a corresponding movement forwards of the sacral plexus.

II. Sacro-coccygeal.—The 30th vertebra forms the 1st coccygeal; not uncommonly this vertebra is sacral in type and forms part of the sacrum [7]. On the anterior or pelvic aspect of the 1st coccygeal vertebra

adaptations to the upright posture. The lumbar curve is most pronounced in the highly civilized races [2].

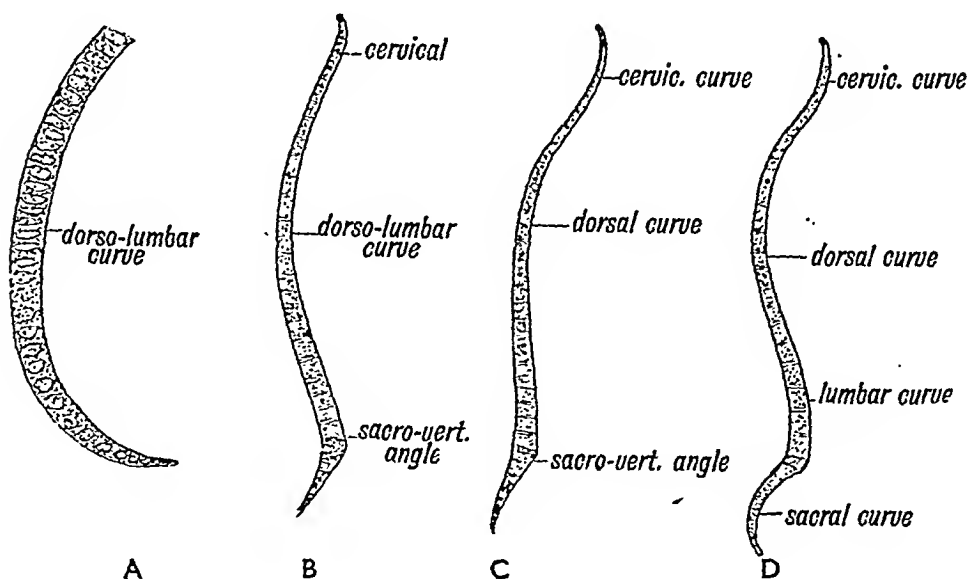


FIG. 64. Diagram of the Curves of the Spinal Column.

A. At the 6th week of foetal life. B. At the 4th month of foetal life. C. Curves present at birth. D. Curves present in the adult.

Proportion of Cartilage and Bone.—The intervertebral discs form one-third of the total height of the spine; the proportion of cartilage is greater in the lumbar than in the dorsal region and greater in the dorsal than in the cervical. The lumbar and cervical curvatures are due chiefly to the shape of the discs. In the lumbar region, which is convex forwards, the lower three vertebrae are deeper in front than behind. This is true only for the civilized races of mankind; in native races, and in the gorilla, only the last lumbar vertebra is deeper in front than behind, and thus helps to maintain the lumbar curvature [3].

Unstable Regions of the Spine [4].—In about 90% of men there are 7 cervical, 12 dorsal, 5 lumbar, 5 sacral and 4 caudal vertebrae, making 33 in all. In the remaining 10% there is some departure from the normal arrangement and these departures affect certain definite regions. The regions affected are those which lie at the junction of one section of the spine with another—at the cervico-dorsal, dorso-lumbar and lumbo-sacral junctions. At an early stage of development all the vertebrae are of the same generalized type; at a later stage the vertebra of each body-segment assumes its peculiar form, but it is not uncommon for one vertebra to assume some or all of the characters of the one before it or behind it. These variations represent the normal error in developmental marksmanship; if the altered aim is advantageous it may become

see the atlas or 1st cervical vertebra partly fused with the occipital bone, representing a tendency to add a 4th vertebra to the occipital series, a condition to be noted in about 1% of skulls (Cave) [9].

It is of interest to know that instability of the vertebral formula is not peculiar to the human body; variations of the same kind and in corresponding regions are to be seen in primates (Schultz), in rabbits (Sawin) and in rats (Frede).

The Notochord.—In its primitive form this predecessor of the vertebral column is well seen during the larval stage of certain fishes (Fig. 50, A). Its manner of origin in the human embryo has been mentioned already (p. 52). The notochord, like the neural canal, is formed from before backwards, beginning under the mid-brain and ending in the last caudal

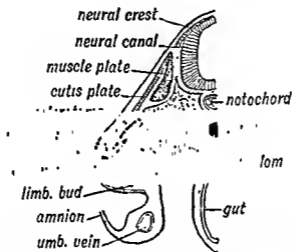


FIG. 67. A schematic section of an Embryo to show the sclerotome, muscle plate and skin plate which arise from each segment of the paraxial mesoderm. (Compare with Fig. 49, p. 50.)

segment. At an early stage it forms a tube, but later becomes a solid rod composed of cells of a peculiar type. A sheath is formed round it by cells of the paraxial mesoderm (Fig. 67), which grow inwards and surround it. These cells, which provide the *Sclerotomes*, spring from the inner parts of the primitive segments or somites into which the paraxial mesoderm is divided (Fig. 67). At the same time the cells of the sclerotomes also grow up and gradually surround the neural tube. From these cells, which grow inwards and surround the notochord and neural canal, the membranous basis of the spinal column is formed and also the basi-occipital and part of the basi-sphenoid bones of the skull (Fig. 68).

• **What becomes of the Notochord [10].**—In the 2nd month of foetal life the notochord begins to disappear; the bodies of the vertebrae and parachordal cartilages form round its sheath and constrict it. The

a rudiment of the *haemal arch* is usually to be found during foetal life. The haemal arches are well developed on the proximal caudal vertebrae of tailed monkeys and represent developments from the hypochordal or intercentral element of a vertebra. Variations at the distal end of the coccyx are dealt with later (p. 569).

III. *Dorso-lumbar region*.—This region is also liable to variation; the 20th vertebra instead of forming the 1st lumbar may simulate the last dorsal in the type of its articular processes, and may bear ribs, probably a reversion to an ancestral condition; or, on the other hand, the 12th dorsal vertebra (19th) may not carry ribs. About 2% of bodies show the latter kind of variation, a reduction of the costal series, and about 6 to 8% the former kind, in which the costal series is increased (see also p. 99).

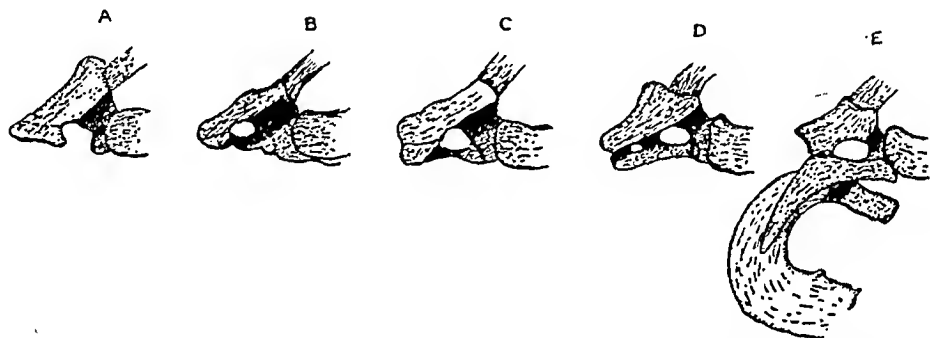


FIG. 66. Diagram showing the variation in the development of the Costal Element of the 7th Cervical Vertebra in 72 skeletons. In A and B the costal element is partly fused with the transverse process; in C, D and E it remains free.

IV. *Dorso-cervical*.—The 7th vertebra may carry ribs; rarely the 8th vertebra has no ribs attached to it and is cervical in type.

In Fig. 66 is represented the condition of the 7th cervical vertebra as seen in a series of 72 human skeletons. In the foetus the costal element is always apparent; in the adult it may vanish or fuse with the transverse process. In about 1% of individuals it assumes the development shown in Fig. 66, E; it may, in occasional cases, assume all the characters of a 1st dorsal rib, with its anterior end implanted on the presternum. Prof. Wingate Todd and others have published a series of observations that confirm the statements made here [8]. A cervical rib may fuse with the costal element of the 1st dorsal vertebra, thus giving rise to a *bicipital* rib (Wood-Jones). The lower trunk of the brachial plexus crosses a *cervical rib*, and hence in such cases symptoms of nerve-pressure may arise.

V. *Cervico-occipital region*.—The occipital or posterior part of the skull represents at least three united vertebrae. Very rarely the last of these may partly assume a vertebral form, but it is by no means rare to

overlies it to become changed into nerve cells and another hormone which "induces" the paraxial mesoderm to become differentiated into the tissues already enumerated [11].

Primitive Segments or Somites.—Somites, or protovertebrae, as they were formerly named, are not the forerunners of the vertebrae; they are the primitive segments into which the mass of mesoderm at each side of the neural canal and notochord divides (Figs. 22, 67). The process of division or segmentation appears in the occipital region at the beginning of the 4th week, and spreads backwards, in rear of the retreating primitive streak, until 35 or more body segments or somites are isolated. Each segment, thus separated, forms its own muscles (from its muscle plate or myotome), has its own nerve (spinal nerve), its own cutis plate

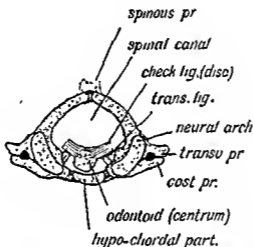


FIG. 70. The morphological parts of the 1st Cervical Vertebra.

or dermatome, and the basis for its skeletal tissue (sclerotome) (Fig. 67). *Intersegmental septa* separate one somite from another. Ribs, transverse and spinous processes are formed in the intersegmental septa. Arteries and veins are intersegmental in position; the hodies of vertebrae are formed by adjacent segments and are therefore intersegmental in origin. Hence an intercostal space with its muscles, vessels and nerves, with the corresponding intervertebral structures, represents a differentiated somite.

Morphological Parts of a Vertebra.—The constituent parts of a vertebra, although much modified, may be best recognized in the atlas (see Fig. 70). These parts are (i) the *centrum*, which forms the odontoid process; (ii) the right and (iii) the left half of the *neural arch*; (iv) the *hypo-chordal part*, which forms the anterior arch or bow. Besides the four chief elements there are three secondary processes or levers, all of which spring from the neural arch. These are (a) spinous, (b) transverse,

parachordal cartilages are transformed into the basi-occipital and part of the basi-sphenoid—the basal part of the skull—behind the pituitary fossa. The notochord disappears in the basilar cartilage of the skull. Eternod, however, found the anterior part of the notochord on the dorsal wall of the pharynx in the human embryo; Robinson has shown that in man the parachordal cartilages are developed in part on its dorsal aspect (Fig. 69). The odontoid process represents the body of the atlas with a remnant of the pro-atlas at its apex (see p. 97), and the suspensory ligament the disc between the occipital bone and the pro-atlas. A

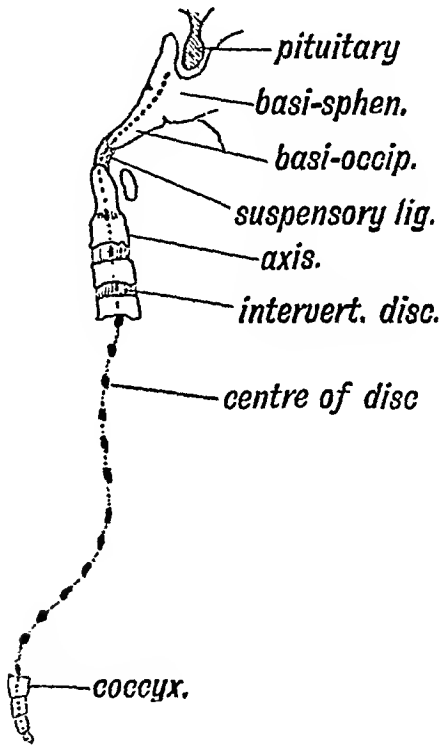


FIG. 68.

FIG. 68. Where Remnants of the Notochord may occur in the adult.

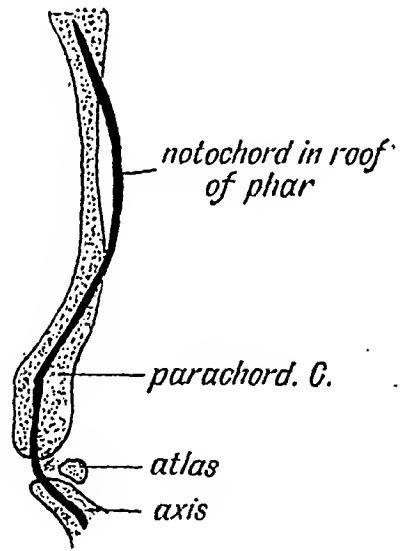


FIG. 69.

FIG. 69. The relationship of the Notochord to the basilar or parachordal cartilage of the human embryo. (Arthur Robinson.)

remnant of the notochord is enclosed in the suspensory ligament. The centrum or body of each vertebra is formed round the notochord (Fig. 72, *F*), but only between the centra, where the intervertebral discs are formed, does this primitive structure persist. In the discs the notochord swells out and forms a considerable part of the central mucoid core (nucleus pulposus) which each disc contains.

The most important function of the notochord has still to be mentioned, its function as an "evocator." As it is being laid down, first in the post-pituitary region and until the tail is reached, it emits a chemical substance or hormone which "induces" the strip of ectoderm which

opposite each intersegmental septum. Hence each centrum must be regarded as the product of two somites. The intervertebral disc is situated opposite the middle of a segment (Ehner). The lateral limbs of the cartilaginous how meet behind (dorsal to) the neural canal in the 4th month, thus completing the neural arch. At the site of a spina bifida (see p. 128) this union fails.

(iii) *Bony Stage*.—The centrum and neural arch elements of the cartilaginous vertebra fuse and give rise to the condition shown in Fig. 72, C. In the 7th week two centres of ossification appear in the centrum, but quickly fuse; one appears in each limb of the neural arch (8th week); at birth the ossific centres of the centrum and neural arch have met.

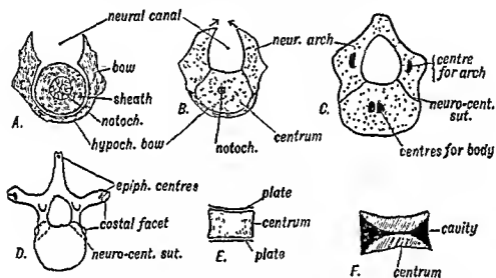


FIG 72 Showing the stages in the development of a vertebra.

A. In the Membranous Stage. B. In the Cartilaginous Stage. C. The appearance of Ossific Points. D. The appearance of Secondary Ossific Centres. E. The Epiphyseal Plates of the Centra. F. Section of an Amphicoelous Vertebra.

The central and neural ossifications meet at the neuro-central suture, and unite at the 4th or 5th year, the *body* being formed by (i) the centrum, (ii) basal parts of the neural arch (Figs. 70, 72). The ossifications of the arch fuse behind (where the spinous process is produced) in the 1st year. The spinous and transverse processes are formed by outgrowths of cartilage into the septa between the somites or primitive segments, where they serve as levers on which the spinal musculature acts. The ribs are also formed by outgrowths from the vertebrae. In the cervical, lumbar and sacral regions they fuse with the transverse processes, but in the dorsal region they remain as separate elements. In typical ribs the head corresponds to the intervertebral disc because, according to Gadov, the rib was originally evolved from an intervertebral element.

(c) costal processes. In the dorsal region the costal processes become separated from the neural arches by articulations ; in other vertebrae they retain their continuity with the arch.

Development of a Typical Vertebra—the 6th Dorsal [12].—(i) Membranous Stage (5th and 6th weeks). The vertebra then consists of two parts, a centrum surrounding the notochord, formed from its sheath (Fig. 71, *A*), and a horse-shoe shaped *vertebral bow* (Fig. 71, *A* and *B*). The membranous centrum is intersegmental in position and is made up of an anterior dense part and a posterior clear part. Wyburn found that the dense part is derived from the segment immediately in front of the centrum ; the clear part, from the segment immediately behind it [13]. The membranous vertebral bow is made up of right and left neural arches,

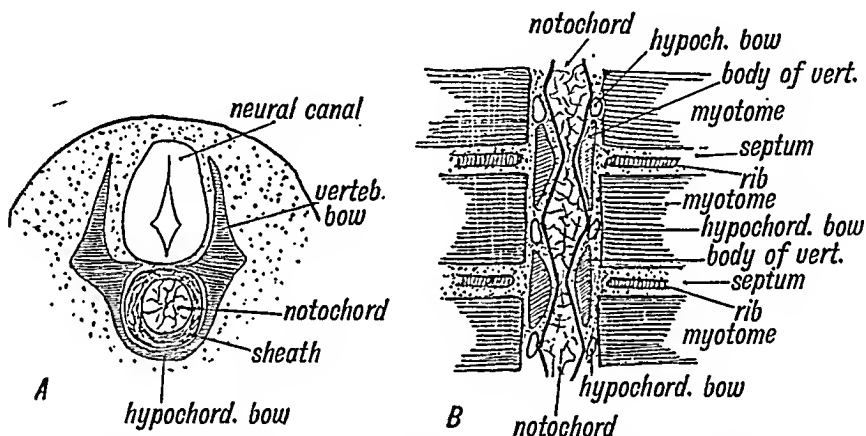


FIG. 71. The development of the Membranous Basis of a Vertebra.

A. In transverse section. *B.* In horizontal section, showing the relation of the vertebra to the primitive segments. The section is viewed from the dorsal aspect.

which are intersegmental in position and become the bases of the bony arches.

(ii) **Cartilaginous Stage** (Fig. 72) commences at the end of the 5th week or beginning of the 6th week, when the embryo is 9 to 10 mm. in length. The fibrous basis of the whole vertebra is transformed into cartilage. In each lateral half of the cellular basis of a vertebra three centres of chondrification appear—one for the neural arch, one for the costal process, and one for each half of the centrum, but those of the centrum soon fuse. In the process of chondrification the cells derived from the sclerotome are directly transformed into cartilage cells. In the atlas the hypochordal part of the bow becomes cartilaginous and subsequently ossified ; in all the other vertebrae, excepting the cervical segments just behind the atlas (Fig. 76), this element never passes beyond the membranous stage of development. It should be noticed (Fig. 71, *B*) that the vertebral bodies are formed round the notochord

while that for the 1st coccygeal appears just after birth, that for the 2nd about the 5th year, and the others at a later date [15].

Occipito Cervical Somites.—In Fig. 74 is given a diagrammatic representation of the three occipital somites and the first three cervical. Only the 3rd occipital (*O.3*) becomes fully developed, the two others to

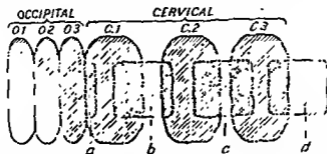


FIG. 74. A diagrammatic representation of the Three Occipital and of the First Three Cervical Segments. (After Gadow.)

O.1, C.1, C.2, C.3, a, b, c, d, represent the elements entering into the composition of the

a slight degree. The 3rd occipital supplies the material for the greater part of the occipital bone. The first cervical segment may be named the pro-atlantal or sub-occipital, as the nerve of this segment (1st cervical) supplies the suboccipital group of muscles. Then follow the atlantal (*C.2*), and axial (*C.3*) segments. Intermediate to the somites are the centra, *a, b, c, d*. A centrum, as we have seen (p. 94), is formed from its own sclerotome and also from that which lies in front. For example, the centrum for the atlas (Fig. 74, *b*) is made up from its own somite (*C.2*) and also from the one which lies in front, the pro-atlantal (*C.1*); similarly for that of the axis (*C.3*). The centrum between *O.3* and *C.1* represents a hemi-centrum belonging to the pro-atlantal segment [16].

In Fig. 75 is depicted the fate of the cervical centra just mentioned. *a* becomes the points of ossification for the odontoid process (*a, a*); *b* becomes the body of the odontoid (*b, b*); *c* becomes the body of the axis. All of these somites have been modified to serve in the sub-occipital movements of rotation and of nodding.

Atlas and Axis.—The atlas represents the completed how of the 1st cervical vertebra (Fig. 70). The body of the vertebra fuses with the

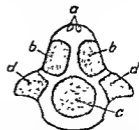


FIG. 75. Body of Axis Vertebra of an Infant, viewed on its anterior aspect, showing the elements entering into its composition.

a, a, pro-atlantal ossific centres; *b, b*, atlantal centres; *c*, centrum of axis; *d, d*, neural arch. (Macalister.)

In atypical ribs—the 1st, 11th and 12th—the head of the rib articulates only with the vertebra behind its own disc. Epiphyseal centres for the ossification of the transverse and spinous processes appear between the 3rd and 4th years.

Bodies of Mammalian Vertebrae are peculiar (*i*) in the development of an upper and lower epiphyseal plate; (*ii*) in that no trace of the notochord remains within them. There being 24 centra between the occiput above and the base of the sacrum below, there are thus 48 cartilaginous plates (epiphyses) at which growth of stature takes place. About the 8th year centres of ossification appear in the periphery of each disc; these separate centres unite to form a ring about the 12th year; the rings become united to their centra from the 20th to the 25th year, when growth in stature is complete [14]. In Fishes, as in the early human or mammalian foetus, the bodies are hour-glass shaped (amphicoelous,

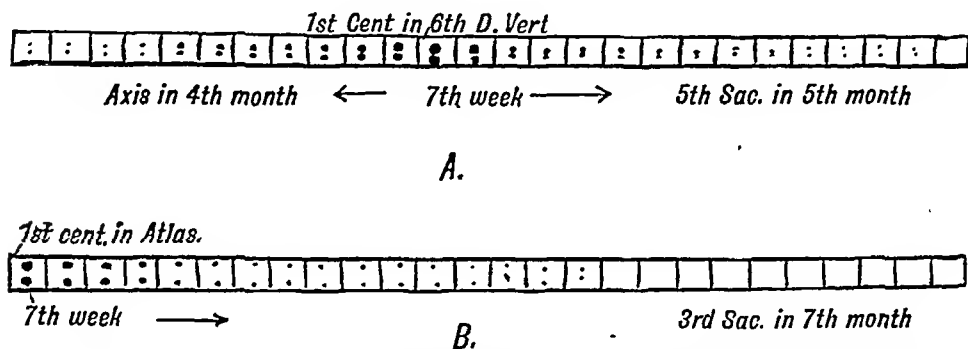


FIG. 73. The order in which the Centres of Ossification appear in the Bodies (A) and in the Neural Arches (B) of the Spinal Column.

Fig. 72, *F*); in Amphibians they may retain a concavity in front (procoelous) or behind (opisthocoelous), but in mammals both ends are filled up.

It will be observed (Fig. 73, *B*) that the *centres of ossification* for the neural arches appear first at the anterior end of the spine (1st cervical), the date becoming later the more posterior the vertebra. In the 1st sacral they appear about the 4th month; in the 2nd sacral, in the 5th month or later; in the 3rd they may not appear. In the 4th and 5th sacral and 1st coccygeal vertebrae only vestiges of the neural arches are formed. These vertebrae retain the early foetus type shown in Fig. 72, *B*. In the remaining coccygeal vertebrae only the centres for the bodies appear. The centres for ossification of the bodies of the vertebrae appear first in the mid-dorsal region (6th dorsal). From that point they spread forwards and backwards, the centres for the odontoid process appearing at the 4th month and that for the 5th sacral at the 5th month,

the embryonic body. In lower vertebrates (birds, reptiles, etc.) each rib has two heads, a dorsal and ventral (Fig. 78). The tuberosity of the human rib represents the dorsal head; the ventral head is well developed in man, as in mammals generally. The rib articulates with the neural arches only (Fig. 72, D). The *conjugal ligament* is made up of fibres which cross in the posterior aspect of the intervertebral disc and unite the heads of the corresponding right and left rib. The conjugal ligament, which is strong in some animals, is weak in man (Bland-Sutton). The transverse ligament of the atlas may belong to the conjugal series.

Vestigial Ribs.—Although the ribs are only fully developed in the dorsal region, yet a representative—a *costal element*—is present in every vertebrae. In the *cervical vertebrae* (Fig. 70) the anterior part of the transverse processes represents a costal process, but only in the 6th (sometimes) and 7th is the costal process formed by a separate centre of ossification. The costal process of the 7th, usually represented by a mere

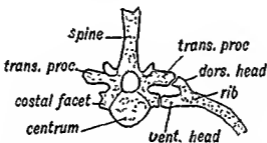


FIG. 78. The Bipartite Rib of a Lower Vertebrate (crocodile)

vestige, may develop into a rudimentary or even a fully formed rib which reaches the sternum (see pp. 90, 580). In the *lumbar vertebrae* only the 1st shows a separate centre for the formation of the costal process: it fuses with the transverse process in the later months of foetal life; in the other lumbar vertebrae the tips or perhaps the whole of the transverse processes represent costal processes. The 12th dorsal rib varies greatly in size; it may be six or ten inches long or reduced to a mere vestige. In quite 40% of women the 12th rib cannot be palpated because it does not project beyond the outer border of the erector spinae.

In the 1st, 2nd and 3rd *sacral vertebrae* the costal processes are large and have their own centres of ossification. Their cartilaginous bases fuse early to form the greater part of the lateral masses of the sacrum. The part of the lateral mass formed by the costal processes is shown in Fig. 80. The costal processes are absent in the 4th and 5th sacral and in all the coccygeal vertebrae. The two lateral epiphyseal plates on each side of the sacrum are new and independent formations.

Accessory processes are found in the lumbar and lowest two dorsal

body of the 2nd, and forms the odontoid process. A remnant of the disc between the atlantal and axial centra can sometimes be seen when the odontoid is split open. The suspensory and check ligaments are the representatives of the disc between the last occipital segment and the pro-atlas (Fig. 74; Fig. 70 and 76). A nodule in the suspensory ligament may represent an occipital centrum (see p. 92).

Occipito-atlanto-axial Articulations.—In the intervertebral discs of the cervical region there is at each side, between the lateral lips of the vertebral bodies, a small articular cavity (Fig. 77). The cavities separate those parts of the cervical bodies which are formed by the neural arches; the spinal nerves issue on the dorsal side of the cavities. Between the axis and atlas this articulation is greatly enlarged. Here the rotatory

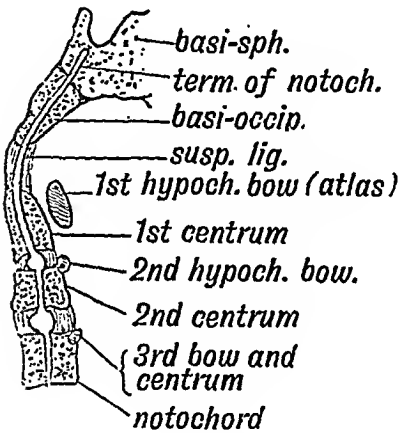


FIG. 76.

FIG. 76. A diagrammatic section of the Foetal Axis, Atlas, and Basi-occipital.

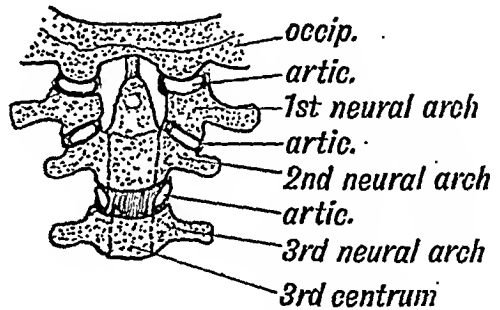


FIG. 77.

FIG. 77. The nature of the Atlanto-axio-occipital Articulations.

movements of the atlas on the axis take place. The atlanto-occipital joint, which separates the atlas and the last occipital segment, is of the same nature. The atlas has neither the upper nor the lower articular processes of the other vertebrae. Hence the 1st and 2nd cervical nerves appear to issue behind the articular processes. At one time the single median occipital condyle seen in birds and reptiles was regarded as very different in nature from the double condyles of mammals. In the lowest mammals (monotremes), the occipital condyles are fused in the middle line; all foetal mammals show this condition. The articular facets on the upper surface of the atlas are also continuous over the hypochordal element. In the human skull a remnant of this median fusion of the condyles is frequently seen on the anterior margin of the foramen magnum; it is named the 3rd or *median occipital condyle*.

The Ribs are developed as outgrowths of the membranous vertebrae into the septa between the primitive segments of the thoracic region of

spinous ligament in the 2nd and 3rd sacral vertebrae. The 2nd, 3rd, 4th, 5th and 6th cervical spines are bifid in Europeans; but in primitive races the 5th and 6th spines are usually undivided; while in anthropoids all the cervical spines are uncleft [19].

Spondylolisthesis.—This name is given to a strange anomaly which affects the neural arch of the 5th lumbar vertebra; occasionally it is seen in the 4th lumbar or 1st sacral. That part of the neural arch which carries the lower articular processes and the spinous process is separated from the rest of the neural arch which carries the upper articular process. In such cases there are on each side of the neural arch two separate centres of chondrification and ossification. When such a developmental anomaly occurs the last lumbar vertebra has no firm hold on the sacrum; its body can slip forwards, carrying with it the whole of the superincumbent spine [20]. Why this anomaly should occur only at the distal end of the lumbar region has not been explained.

Caudal or Coccygeal Vertebrae.—At the end of the 6th week, the body of the embryo being then about 11 mm. in length, the human tail reaches its maximum growth—projecting as a conical process fully 1 mm. in length and equal to about one-tenth of the long diameter of the embryonic body. In the adult body the 30th vertebra is usually the first of the coccygeal series. In the 5th week the growing caudal point, at which neural canal, notochord, sclerotomes, and cloaca are all being extended in a backward direction, has reached and produced the 30th segment (Fig. 81); at the 6th week, 10 or 12 caudal segments have been laid down. Thereafter retrogression sets in; by the end of the 8th week (Fig. 81) only the caudal tip projects and the coccygeal vertebrae have been reduced to 4 or 5; while by the 13th week a depression or pit marks the site where the tip disappeared. The coccygeal part of the neural canal is atrophied and the distal part of the whole cord is retracting in a cranial direction [21]. The coccygeal vertebrae chondrify during the 5th and 6th weeks; the 1st begins to ossify just after birth, while the centre for the last appears about puberty [22]. A submerged tail may be formed [23]; caudal development is even more reduced among the anthropoid apes than in the human family [24].

Irregular Segmentation.—As growth extends the embryonic plate backwards, laying down new tissue as it proceeds, division after division appears in the newly formed paraxial mesoderm, thus separating it into segments. Each new segment contains a set of developmental potentialities which differ from the set contained in the preceding segment; the segment which is supplied by the ventral root of the 11th cervical nerve (the 11th somite), for example, has not the same set of potentialities as that included in the 1st dorsal (12th somite).

vertebrae. They are developed at the base of the transverse processes and are for the attachment of slips of the longissimus dorsi. Each is completed by a separate centre of ossification; that on the transverse process of the 5th lumbar may simulate a fracture in a radiogram (H. A. Harris) [17]. The *mammillary processes*, which are also completed by separate centres of ossification, are developed on the articular processes of the lower two or three dorsal and all the lumbar vertebrae. They give attachment to tendons of origin of the multifidus spinae. Prof. Wood-Jones has pointed out that these two muscular processes, the mammillary and accessory, are fused together in the dorsal region, but in the lumbar region they are separated by a groove containing the

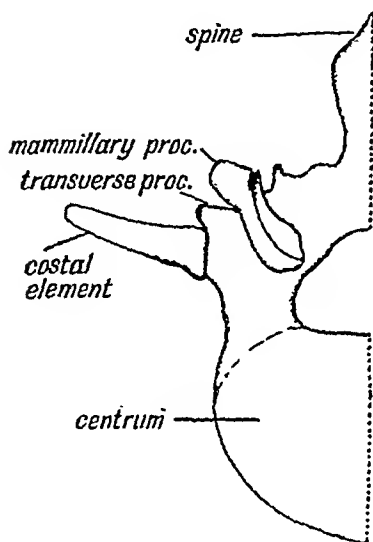


FIG. 79.

FIG. 79. Half of a 1st Lumbar Vertebra showing a separate Costal Element.

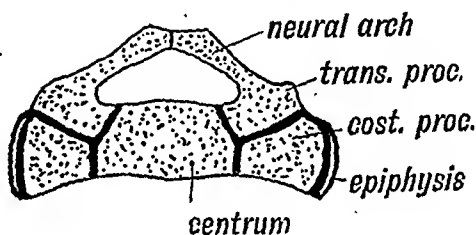


FIG. 80.

FIG. 80. A section to show the nature of the Elements composing the Sacrum.

inner branch of the posterior division of the corresponding spinal nerve [18].

Transverse and Spinous Processes grow out from the vertebral bow (Fig. 72, A) into the septa between the primitive segments. Each transverse process is pierced, while still in the membranous condition, by a branch of the corresponding segmental (intercostal) artery. In only the cervical region do those perforating arteries and their foramina persist. In that region the perforating arteries anastomose, and out of the chain thus formed is developed the vertebral artery. Thus the foramina for the vertebral artery are formed independently of the costal element in each cervical transverse process. Spinous processes are absent from the 1st cervical, 4th and 5th sacral and coccygeal vertebrae. They are slightly developed and united by ossification of the inter-

this anomaly the scapula is placed higher than usual and is bound to the spinal processes of the cervical vertebrae or to the occiput by a fibrous or bony band, recalling the condition found in certain fishes (selachian).



FIG. 82 Cervical and dorsal parts of the Spine of a Human Foetus showing irregularities of segmentation.

NOTES AND REFERENCES

[1] For dates at which children learn to stand, walk, speak, etc., see Variot and Goteu, *Bull. et Mem. Soc. d'Anthropol.*, 1937, 8, 17. (Three out of every four children learn to walk after the 11th month and before the 15th.)

[2] Blume, W., *Zeitsch. Anat. u. Entwickl.*, 1934, 103, 498; Bleicher and Beau, *Compt. Rendu. Ass. Anat.*, 1932, 27, 37.

[3] Cunningham, D. J., *Cunningham Memoirs* (No. 2), Royal Irish Acad., 1886; Martin, R., *Lehrbuch der Anthropologie*, 1928 (2nd ed.).

[4] From the 20th to the 30th day the dorsal axis of the human embryo is the scene of two active developmental processes: the notochord is being formed and submerged and, as it is being formed, the mesoderm on each side of it becomes separated into segments or somites. This dual process begins in the occipital region of the head and ends in the sacro-coccygeal region. To account for what is seen to take place the embryologist postulates two factors. The first factor relates to the paraxial mesoderm; he assumes that this tissue, at its first development, is endowed with certain developmental capabilities or "competences," these changing in nature as the paraxial tissues are followed backwards in the embryonic body. The second assumption relates to the notochord; it is assumed, as it is laid down, to be charged with hormones which evoke local centres of differentiation in the blocks of paraxial mesoderm lying on each side of it. In each local centre, or somite, the paraxial "competences" are called into being. One is apt to think of somites as so many slices cut off from the paraxial "loaf," the intersomitic septa or partitions being primary, whereas they are the undifferentiated tissue which separates the local centres of differentiation. For the bases of such assumptions, see Needham's *Biochemistry and Morphogenesis*, 1942.

[5] The literature on the anomalies and malformations of the human spinal column is enormous; only some of the more recent papers are cited here. Knehe.

The lines of cleavage separate one set of potentialities from another. It can therefore be understood that cleavage lines may vary in their incidence; the cleft which cuts off the 12th somite from the 11th may vary so that something which goes usually to the 11th somite is retained in the 12th, or vice versa. This example will serve to illustrate what is meant by *normal* or *functional irregularity* [25]. During the period of segmentation, or for part of that period, the embryo may be subjected to injurious conditions. *Abnormal* or *pathological peculiarities* may then be produced: segments may separate irregularly, so that two or three ribs are conjoined; or a segment may be present on one side of the body

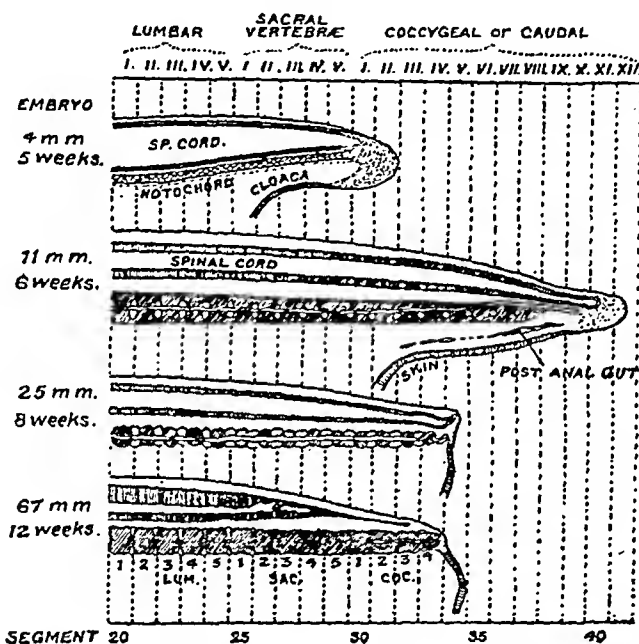


FIG. 81. A series of four figures showing the condition of the Human Caudal or Coccygeal Region at the stages indicated on the drawings. (After Kunitomo.)

and not on the other; half a vertebra may be missing; the vertebrae of the neck may show varying degrees of fusion. With irregular segmentation of the trunk, developmental anomalies are usually found in the vascular and alimentary systems [26]. In Fig. 82 are depicted the spinal column and the costal series of a foetus in which there has been marked irregularity in the demarcation of the primary segments. The vertebrae of the 3rd and 4th cervical segments are fused on the left side; succeeding segments show abnormalities of a similar kind. The 2nd and 3rd ribs of the right side are unseparated. In the same foetus the pectoral muscles were defective. With such irregularities of segmentation of the cervical region, there is often combined a strange anomaly of the shoulder known as *congenital elevation of the scapula*. In children showing

observers find that there is a separation of the 5th neural arch in about 5% of cases examined. In a similar proportion of cases the neural arches of L, V, or S, I, fail to meet in the mid-dorsal line, a condition which has received the name *spina bifida occulta*.

[21] For development of caudal segments, see Streeter, G. L., *Amer. Jour. Anat.*, 1919, 25, 1; Kunitomo, K., *Contrib. Emb.*, 1918, 8, 161.

[22] For chondrification and ossification of coccygeal vertebrae, see under Diculafé, R., note [15].

[23] Reynolds, R. J., *Brit. Jour. Radiol.*, 1932, 5, 457.

[24] See references under Schultze, A. H., note [6].

[25] See note [4].

[26] For examples of irregular segmentation, see Harris, H. A., *Jour. Anat.*, 1923, 57, 76; Wakeley, C. P. G., *ibid.*, 1923, 57, 147; Feller and Sternberg, *Zeitsch. Anat. Entwickl.*, 1934, 103, 608. In the condition described as *Dysplasia foetalis* there are often irregularities of segmentation (see Chapter IV, p. 73).

K., *Zeitsch. Morph. u. Anthropol.*, 1936, 35, 1-376 (X-ray examination of 108 pairs of twins, 52 of the pairs being identical); Brailsford, J. F., *Brit. Jour. Surg.*, 1929, 16, 562; *The Radiology of Bones and Joints*, 1934; Willis, T. A., *Jour. Bone Joint Surg.*, 1932, 14, 267; Fischer, H., *Les Dymorphies du Rachys*, 1929; Junghans, H., *Zeitsch. Anat. Entwickl.*, 1937, 106, 625 (gives full literature); Shore, L. R., *Jour. Anat.*, 1930, 64, 206; Bardeen, C. R. (1871-1935), *Amer. Jour. Anat.*, 1905, 4, 163; Rosenberg, E., *Morph. Jahrb.*, 1907, 36, 609.

[6] Keith, Sir A., *Jour. Anat.*, 1903, 37, 18 (evolutionary changes in vertebral formulae of higher primates); Schultz, A. H., *Amer. Jour. Phys. Anthrop.*, 1938, 24, 1; *Anat. Rec.*, 1938, 70, 70; *Human Biol.*, 1930, 2, 303 (dealing with vertebral formulae and vertebral variations in the higher primates).

[7] Dieulaufé, R., *Archiv. Anat.*, 1933, 16, 43 (records observations on 130 bodies, in 22 of which the 1st coccygeal was united to sacrum).

[8] Todd, T. W., *Jour. Anat.*, 1912, 46, 244; Wood-Jones, F., *ibid.*, 1911, 45, 249; Cave, A. J. E., *ibid.*, 1930, 64, 116; Dow, D. R., *ibid.*, 1925, 59, 166 (D, I, with vestigial ribs); Gladstone and Wakeley, *ibid.*, 1932, 66, 334 (a similar case).

[9] For recent literature on occipito-cervical anomalies, see Bystrow, A. P., *Zeitsch. Anat. Entwickl.*, 1934, 102, 307 (full literature); Heidsieck, G., *Anat. Anz.*, 1931, 72, 113; Latarjet, M., *Ann. d'Anat. Path.*, 1936, 13, 749; Gladstone and Wakeley, *Jour. Anat.*, 1925, 59, 195; Green, H. L., *ibid.*, 1931, 65, 142; Cave, A. J. E., *ibid.*, 1930, 64, 337; 1934, 68, 521; Hunter, R. H., *ibid.*, 1924, 58, 140. For cases of partial separation of 3rd occipital segment, see Sauser, G., *Zeitsch. Anat. Entwickl.*, 1934, 102, 51; 1935, 104, 159.

[10] See note [16], Chapter I.

[11] See Needham's *Biochemistry and Morphogenesis*, p. 160.

[12] For development of vertebrae, see Bardeen, C. R., *Amer. Jour. Anat.*, 1908, 8, 181; Wyburn, G. M., *Jour. Anat.*, 1944, 78, 94. For morphology of vertebrae, see *The Evolution of the Vertebral Column*, by the late Dr. Hans Gadow, edited by Gaskell, J. F., and Green, H. L., 1933.

[13] Wyburn, G. M., see reference under note [12].

[14] For anatomy of intervertebral discs, see Beadle, O. A., *Rep. Med. Resear. Coun.*, 1931, No. 161; Coventry and Others, *Jour. Bone and Joint Surg.*, 1945, 27, 27, 233; Keyes and Edward, *ibid.*, 1932, 14, 897; MacGowan, T., *Lancet*, 1, 258 (epiphyseal plates of centra); Cave, A. J. E., *Proc. Zool. Soc. Lond.*, 1934, 2, 225.

[15] For ossification of vertebrae, see Harris, H. A., *Brit. Jour. Radiol.*, 1933, 6, 685; MacGowan, T., *Lancet*, 1, 258; for ossification of coccyx, see Dieulaufé, R., *Archiv. Anat.*, 1933, 16, 543.

[16] Gadow, H. (see note [12]); Cave, A. J. E., *Jour. Anat.*, 1938, 72, 621.

[17] See Harris, H. A. (note [15]); Cave, A. J. E., *Jour. Anat.*, 1936, 70, 275; 1937, 71, 497; Odgers, P. N. B., *ibid.*, 1933, 67, 301 (characters of articular processes of lumbar vertebrae).

[18] Wood-Jones, F., *Jour. Anat.*, 1912, 47, 118.

[19] Shore, L. R., *Jour. Anat.*, 1933, 67, 422; 1931, 65, 482; Cave, A. J. E., *ibid.*, 1931, 65, 171; Mijsberg, W. A., *Zeitsch. Anat. Entwickl.*, 1926, 79, 112.

[20] For literature on Spondylolisthesis, see references under Brailsford, Willis, Fischer and Junghans, note [5]; Bohart, W. N., *Jour. Amer. Med. Ass.* 1929, March 2; Stewart, T. D., *Amer. Jour. Phys. Anthrop.*, 1933, 17, 123 (amongst Eskimo; in a series of natives from the same area this condition occurred in over 20%); Capener, N., *Brit. Jour. Surg.*, 1932, 19, 374; Young, M., and Hastings Ince, J. G., *Jour. Anat.*, 1940, 74, 369 (examination of 510 young women). Most

the distribution of nerves have shown that it has a direct bearing on diagnosis and treatment.

Constitution of a Typical Segment (11th Dorsal).—It is better to study the development of a typical body segment, and from this students will be able to note for themselves the modifications which have taken place in the more highly differentiated segments of the body. As already explained, the process of segmentation affects chiefly the paraxial block of mesoderm which lies on each side of the neural canal and notochord, and also, to a lesser degree, the intermediate cell mass. In Fig. 84, *A*, *B*,

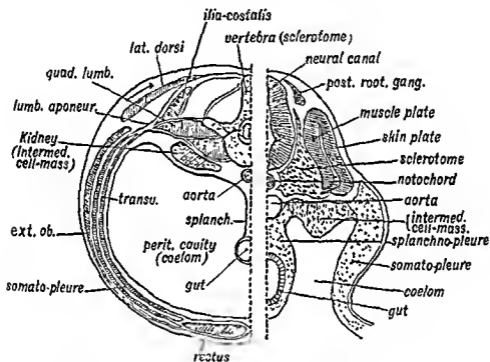


FIG. 84.

A. A Transverse section showing the Elements of the 1st Lumbar Segment in the Adult.

B. A corresponding section of an Embryo about the end of the 4th week (diagrammatic).

a body segment is represented in the adult and in the embryonic condition.

The following elements make up the 11th dorsal segment: (i) Its skeletal basis; (ii) Muscular element; (iii) Renal element; (iv) Vessels; (v) Nerves; (vi) Neural segment; (vii) Cutis plate. Although the ectoderm and endoderm are never segmented, yet a definite area of each is associated with every body segment. The origin of each element will be taken separately.

1. The *skeleton* of the 11th dorsal segment is represented by the adjacent halves of the 11–12 dorsal vertebrae and the disc between them, for, as already pointed out, the vertebrae are intersegmental in their

CHAPTER VII

THE SEGMENTATION OF THE BODY

At the beginning of the 4th week, as we have already seen (p. 60), the paraxial mesoderm lying at each side of the neural tube becomes divided from before backwards into somites or primitive segments, their demarcation being evident first in the occipito-cervical region of the body. By the end of the 4th week the process has reached the 1st coccygeal segment, there being then 3 occipital and 30 body somites. The occipital somites soon lose their identity, but those of the body, although they become specialized and broken up, can still be recognized

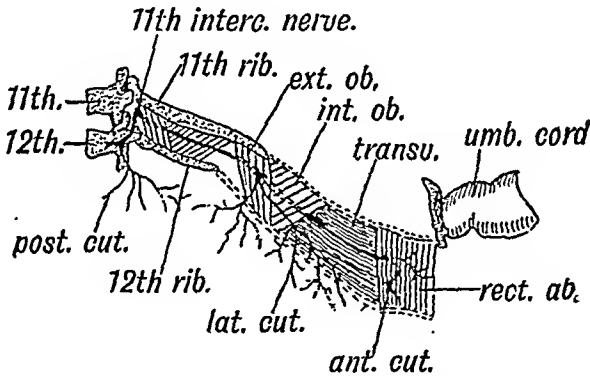


FIG. 83. Some of the Structures derived from 11th Dorsal Segment of the Right Side.

in the adult. In the preoccipital region of the head, parts are also arranged on a segmental plan, one which is older than the vertebrate segmentation of the trunk and can best be identified by the visceral or gill arch system of the pharynx (see p. 345).

Segmentation of the Body.—The human body or trunk consists of 33 or 34 segments. Each segment is fundamentally of the same type, but the resemblance is obscured owing to extensive modifications which the somites undergo to form the cervical, dorsal (thoracic), lumbar (abdominal), sacral (pelvic) and caudal regions of the body. The outgrowth of the limbs also renders it difficult to recognize in the adult the simple system of segments which can be seen in the embryo at the end of the 4th week (Fig. 23, p. 24).

Until lately the segmentation of the human body has been a matter of only speculative importance, but recent advances in our knowledge of

The ventro-lateral sheet separates into a *ventral longitudinal* band and a lateral transverse-oblique stratum. Each of these divides into an inner and outer *primary* layer; the outer and inner *secondary* layers arise as delaminations of the primary layers, thus making four in all. The internal oblique and transversalis and internal intercostal are derived from the internal primary layer; the external oblique and external intercostal from the external primary layer. The rectus abdominis represents the deeper of the two layers derived from the external primary; as we shall see later (p. 590) its segmentation arises in a secondary manner. Parts of the deepest layer of the lateral sheet, represented in the adult by the transversalis, have migrated inwards to form the subvertebral or *hypaxial* muscles—the quadratus lumborum, crura of the diaphragm, longus colli, rectus capitis anticus major and minor and the levator ani. When muscles migrate they carry with them the nerves of the body segments in which they are developed. Hence the nerve supply affords a clue to the segments from which a muscle or part of a muscle arises [5]. The middle layer of the lumbar fascia is developed between the epaxial and ventro-lateral musculatures.

Many of the ventro-lateral muscles (trapezius, rhomboids and latissimus dorsi) migrate dorsalwards over the epaxial muscles, and take origin from the spines of the vertebrae (Fig. 84, A).

Muscular fibrillae begin to form in the 5th week, appearing in the protoplasmic matrix, in which the nuclei of the *myoblasts* are embedded. The fibrillae group themselves in bundles or muscle fibres, the nuclei with some of the myoplasm being applied to the surface of the completed fibre. New fibre production goes on rapidly until the 5th month, when the complement for each muscle is nearly complete (see also p. 588). Thereafter muscles grow in size, chiefly, it is believed, by an increase in the size of the individual fibres. Although voluntary muscle fibres atrophy when their nerve is cut, yet myoblasts will develop into muscles when separated from nerve cells (Ross Harrison) or when grown in artificial media outside the body [1].

III. *Arteries of the 11th Segment* (Fig. 85).—Arteries are intersegmental in position; hence the 11th segment has really two arteries and two veins—the 10th and 11th intercostals [6]. We shall describe the 11th intercostal as a type. It gives off a dorsal branch to supply the epaxial muscles, the spinal column, spinal cord and membranes, and skin. The segmental artery joins at its termination with a ventral longitudinal vessel, the deep epigastric. The primitive arrangement in vertebrates appears to have been one with a dorsal and ventral longitudinal vessel, the segmental artery passing from the dorsal to the ventral vessel. The vertebral, ascending cervical, deep cervical,

development (Fig. 71, *B*). The transverse processes, the spinous processes and 11th and 12th ribs are also formed in the septa in front of and behind the 11th segment (Fig. 83). The septum in the rectus muscle a little below the umbilicus represents the intersegmental septum corresponding to the 11th rib. Sometimes another septum occurs in the rectus, midway between the pubes and umbilicus, marking the lower limit of the 11th segment. The linea alba separates the segments of the two sides.

In the linea alba, or ventral median line of the thoracic region, the sternum is developed. The intersegmental septa are well marked in the thoracic region; the ribs and their cartilages are developed in them. In the neck the septa are almost lost; the intermediate tendon of the omohyoid and the septa occasionally found in the sterno-hyoid and sterno-thyroid, complexus and trachelomastoid muscles are the only representatives of them in the cervical region.

II. *The Muscles of the 11th Dorsal Segment.*—All the muscles of this segment are developed from the muscle plate (myotome) of the primitive segment (see Figs. 83 and 84). There is a cavity in each primitive segment (Fig. 49, p. 59). The cells of the mesoderm on the inner side of the segmental cavity become columnar and form the muscle plate (Figs. 67, 84). Each segment has its own muscle plate. The cells or *myoblasts* of each plate increase rapidly in number, forming a fused mass or syncytium; they spread into the somatopleure, and form the muscles of the body-wall and limbs (see also p. 579). In the myosyncytium, fibrillae and fibres are formed; each fibre, which, although multinucleated, represents a single cell, becomes elongated and directed across its segment from septum to septum [1]. The intercostal muscles retain this arrangement [2], but in the abdominal region the fibres fuse with those of neighbouring segments to form muscular sheets—the external oblique, internal oblique, transversalis and rectus. In the foetus of the 5th month traces of these septa may be seen; Bardeen found that the intercostal nerves retained their segmental distribution in the muscles of the belly-wall [3]. In fishes the embryonic segmental arrangement of the musculature persists. The manner in which the final groups of muscles are derived from the muscle plates is not accurately known, but in the typical segment with which we are at present dealing it will be seen that the musculature falls into two groups (see Fig. 84, *A*); (i) *epaxial*, the erector spinae, etc.; and (ii) *ventro-lateral* or body-wall muscles (intercostals, rectus, oblique muscles, etc.). The musculature of the limbs, although developed directly from the mesenchyme of the limb bud, yet in a morphological sense must be classified with the ventrolateral group [4].

cells arise: (i) somatic motor, (ii) somatic sensory, (iii) splanchnic motor, (iv) splanchnic sensory. The splanchnic motor cells for the greater part remain within the spinal cord, but many enter sympathetic ganglia; the sensory groups are included in the posterior root ganglia [7]. The nerve fibres connected with the somatic groups have a diameter varying from $9-18\mu$; those with the splanchnic, $2-9\mu$. The *somatic motor* group, in the anterior horn, sends out processes to all the muscles of the primitive body segment in which it is situated. The anterior root of a spinal nerve is formed by the somatic motor fibres. The *splanchnic motor* cells, in the lateral horn, send out processes into the

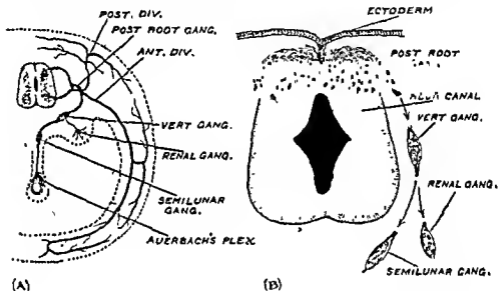


FIG. 86.

A. Diagram of the Nerve System of the 11th Dorsal Segment

B. A diagram showing the derivation of the Parts of the Nerve System of the 11th Segment in the Embryo.

splanchnopleuric which reach viscera through the white rami communicantes and sympathetic system (Fig. 86, A).

The segmentation of the spinal cord, as manifested by the serial arrangement of its nerves and ganglia, is secondary to the segmentation of the paraxial mesoderm. If the segmentation of the mesoderm is hindered or altered by experiment, then the serial arrangement of nerves and ganglia is also altered [8].

At the point where the medullary plates are cut off from the ectoderm to form the neural canal, a crest, the *neural crest*, grows out on each side (Fig. 86, B) composed of the cells which were included in the junctional line between medullary plates and ectoderm. A group of these neuroblasts—the *somatic and splanchnic sensory* cells—grows into each seg-

ascending lumbar and lateral sacral arteries are examples of the anastomoses that may arise between segmental arteries.

Segmental arteries also arise from the aorta to supply the structures formed from the intermediate cell mass (the kidney, testis, ovary, etc., Fig. 85). As a rule only one renal segmental artery persists, but frequently accessory renals are seen. These may be persistent embryonic vessels of several segments of the intermediate cell mass in which the Wolffian body and kidney arise. The splanchnopleure shows no certain traces of segmentation; hence its vessels (coeliac axis and mesenteric) if of segmental origin have become profoundly modified. Broman has

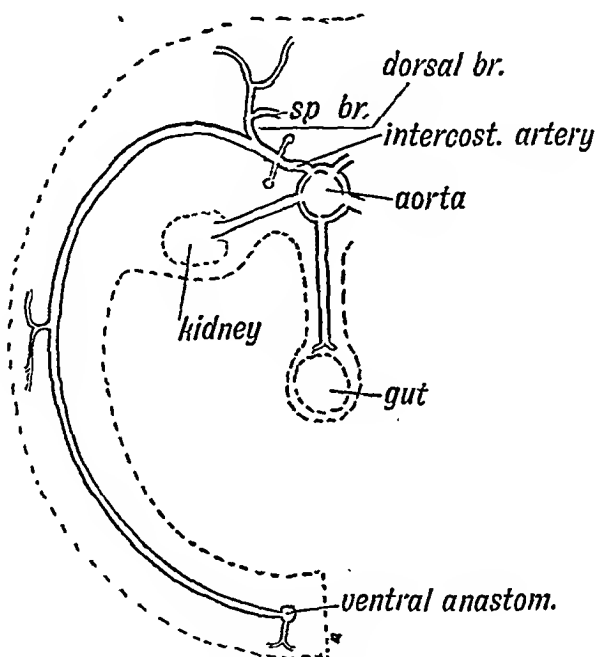


FIG. 85. The distribution of a typical Somatic Artery.

demonstrated that the splanchnic arteries have the appearance of a segmental arrangement in the embryo (Fig. 29). During the 4th week there are right and left aorta, each giving off splanchnic branches; in the 5th week fusion of the aortic trunks sets in; later the right and left splanchnic branches unite.

IV. *Nerve Elements of the 11th Segment* (Fig. 86).—Although the spinal cord during development of the human embryo shows no outward sign of being divided into segments corresponding to those of the body, yet from what we know of its condition in embryos of lower animals and from clinical evidence there can be little doubt that such a serial grouping does take place, and that the cord is demarcated, in a functional sense, into segments corresponding to those of the body. From each segment, extending from D.1 in front to L.2 behind, four groups of

cells arise: (i) somatic motor, (ii) somatic sensory, (iii) splanchnic motor, (iv) splanchnic sensory. The splanchnic motor cells for the greater part remain within the spinal cord, but many enter sympathetic ganglia; the sensory groups are included in the posterior root ganglia [7]. The nerve fibres connected with the somatic groups have a diameter varying from $9-18\mu$; those with the splanchnic, $2-9\mu$. The somatic motor group, in the anterior horn, sends out processes to all the muscles of the primitive body segment in which it is situated. The anterior root of a spinal nerve is formed by the somatic motor fibres. The splanchnic motor cells, in the lateral horn, send out processes into the

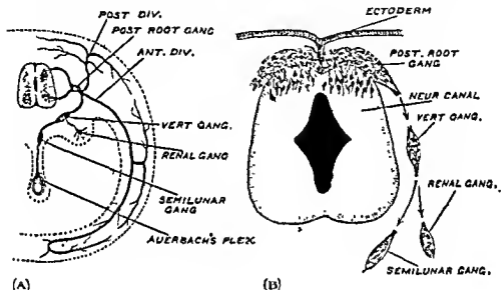


FIG. 86.

A Diagram of the Nerve System of the 11th Dorsal Segment.

B A diagram showing the derivation of the Parts of the Nerve System of the 11th Segment in the Embryo.

splanchnopleure which reach viscera through the white rami communicantes and sympathetic system (Fig. 86, A).

The segmentation of the spinal cord, as manifested by the serial arrangement of its nerves and ganglia, is secondary to the segmentation of the paraxial mesoderm. If the segmentation of the mesoderm is hindered or altered by experiment, then the serial arrangement of nerves and ganglia is also altered [8].

At the point where the medullary plates are cut off from the ectoderm to form the neural canal, a crest, the *neural crest*, grows out on each side (Fig. 86, B) composed of the cells which were included in the junctional line between medullary plates and ectoderm. A group of these neuroblasts—the *somatic and splanchnic sensory cells*—grows into each seg-

ment and forms the *posterior root ganglion*. Each neuroblast within the ganglion sends out a process which bifurcates, one branch or fibre growing into the cord and ending in the posterior column and cells of the posterior horn, the other passing to the skin, muscles, etc., of the segment. The posterior nerve root is thus formed by the ingrowing processes from the cells of the posterior root ganglion, and the body segment in which the outgrowing processes are distributed is thereby brought into sensory communication with the central nervous system (see also p. 124). The anterior and posterior roots unite to form a spinal or segmental nerve. Like the artery, it divides into a posterior division for the epaxial part of the segment and an anterior for the ventro-lateral part (Fig. 86, *A*). The *splanchnic sensory* groups are situated in the posterior root ganglia.

The cells of the sympathetic system, derived chiefly from the neural crest and, to a lesser extent, from the anterior horn, form a continuous column on each side of the spine at their first appearance (5th week). From these two paravertebral columns are differentiated :

- (a) The prevertebral ganglion situated on the vertebra (in the gangliated chain), ventral to the exit of the spinal nerve ;
- (b) A group to the intermediate cell mass (renal ganglion and adrenal body) ;
- (c) Another to the splanchnopleure (semilunar ganglia) ;
- (d) To the viscera (cells of Auerbach's plexus, etc.).

Groups (c) and (d) show no trace of segmentation in their arrangement, but, clinically, evidence is to be found that every viscus or part of a viscus is connected with certain segments of the spinal cord.

The manner in which the cells or neurons of the ganglia are connected with the spinal cord is shown diagrammatically in Fig. 87. The motor or efferent fibres issue by the anterior roots (from D.1 to L.2) to terminate round a cell or cells in any one of the ganglia or cell-groups just mentioned (*a, b, c, d*). Thus these fibres link the splanchnic motor stations in the cord to all sympathetic ganglia. In their turn ganglion relay cells send processes to end round muscular or secretory cells. Thus a neuron is always interposed between the fibre emerging from the cord and the actual site at which the motor or secretory impulses are delivered. On the other hand, the sensory splanchnic cells which are included in the posterior root ganglia collect their stimuli in the tissues and deliver them direct to the recipient centres in the cord. Both afferent and efferent fibres after issuing in the anterior and posterior roots pass to their ganglionic terminations by the *white rami*. In this manner certain segments of the spinal cord are brought into touch with certain tissues and organs within the body cavities. The vaso-motor supply of each

body segment passes to it from the sympathetic ganglion by a grey ramus communicans [9].

It will thus be seen that all the parts of a segment—body-wall (somatopleure), kidney (intermediate cell mass) and a part of the abdominal or thoracic viscera (splanchnopleure)—are connected by nerves to a corre-

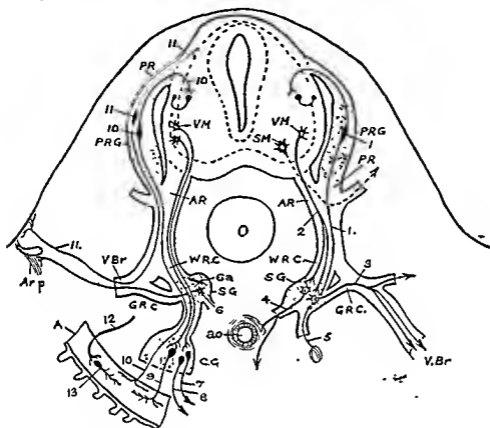


FIG. 89. Diagram of a body segment showing the internal organs and their neural connections.

A.R., anterior root; *P.R.*, posterior root; *P.R.G.*, posterior root ganglion; *V.M.*, viscero-motor cell; *S.M.*, somatic motor cell; *W.R.C.*, white ramus communicans; *G.R.C.*, grey ramus communicans; *V.Br.*, ventral branch of spinal nerve; *Ar.*, aorta; *A*, piece of wall of intestine; *Ar.P.*, arrector pili.

sponding segment of the spinal cord. In diseased conditions of any part of a body segment, the corresponding spinal segment of the cord is disturbed. Such a disturbance is referred along the somatic sensory fibres, giving rise to areas or zones of **hyperaesthesia**. Thus, for instance,

a stone in the pelvis of the kidney (which is supplied from the 10th, 11th and 12th dorsal segments) is frequently accompanied by pain which becomes manifest along the XIth and XIIth intercostal nerves. In the central nervous system as in the muscular, the primary simple segmental arrangement has been disturbed by enormous changes which have occurred in the process of evolution. In order to secure a harmonious co-operation of the various segments of the body, communications have been established, by means of nerve tracts, between the various segments of the spinal cord and between the segments of the cord and the higher centres of the brain. These communications have obliterated wellnigh all traces of primitive segmentation, and yet we see in the ganglia of the posterior roots and in the prevertebral ganglia of the sympathetic chain clear evidence that each segment of the body was originally provided with its own semi-automatic nerve mechanism. Clinical observation has supplied evidence that certain viscera—such as the heart, the liver, the kidneys—have a nervous correlation with certain segments of the body, and we may infer that these organs have been evolved in connection with certain definite segments of the body.

Segments from which Splanchnic Fibres escape.—The small medullated or splanchnic fibres do not arise from every spinal segment. Bishop Harman found that in man such fibres escape only by the roots of the dorsal nerves and 1st lumbar; occasionally splanchnic fibres come out in the roots of the last cervical and 2nd lumbar [10]. These fibres enter the gangliated chain, and are distributed to the viscera. Splanchnic fibres also escape by the 3rd sacral, frequently too from the 2nd or 4th, to form the *nervi erigentes* for the pelvic viscera. The greater part of the IXth, Xth and XIth cranial nerves is made up of splanchnic fibres. There are thus three visceral areas—an anterior or medullary, a middle or thoracic and a posterior or sacral. How these centres came to be thus separated is not known [11]. It is also remarkable that the nerve centres which regulate or constrict arterioles are situated in the middle or thoracic area.

Protopathic and Epicritic Systems.—In the 11th dorsal segment, as in all segments of the trunk, two systems of somatic sensory nerves have to be recognized—both of which have their cell-stations in the ganglia of the posterior roots. There is, in the first place, the system to which Head gave the name *protopathic* and for which Stopford [12] proposes the name *protective*. This represents the older system of sensory nerves. Its fibres on entering the spinal cord are relayed to the opposite side, their messages being carried in the spino-thalamic tract to centres in the optic thalamus. Head's second or *epicritic* system, the *discriminative* system of Stopford, ascends in the posterior column of the cord on the

side of entry, their messages ultimately reaching the sensory cortex of the opposite side, where they are "discriminated" and analysed. Section of a posterior root produces loss of protopathic sensation of the corresponding segment of the body; the protopathic system is segmental in its distribution. The distribution of vaso-motor nerves is also segmental. Epicritic nerves, on the other hand, are not confined to their proper segments, but invade the territory of neighbouring segments (Stopford).

In revising the present edition (1946) I have left the preceding paragraph unchanged as a record of a theory which is now given up by most neurologists. The protopathic system was regarded as the original sensory outfit, into which a later and higher system had been grafted—the epicritic. This dual sensory system was postulated to explain the order in which sensation returned to an area of skin which had been deprived of its nerve-supply. The power to feel pain returned first; that of precise localization of touch and pressure last. Modern neurologists account for the order in which sensation returns by postulating not two sensory systems, but by the observed fact that the non-medullated fibres which serve pain-stimuli are the first to be regenerated, while those which subserve touch are the last [13]. Dr. Weddell noted that points in the skin which serve as the source of touch stimuli receive a supply of fibres from several adjacent nerves [14]; it is this multiple supply which provides the cortex with the data needed for precise localization. Thus modern neurologists regard the sensory system as having been evolved as a unity, not as a duality.

NOTES AND REFERENCES

- [1] For differentiation of voluntary muscle fibres, see Speidel, C. C., *Amer. Jour. Anat.*, 1938, 62, 179; Cuajunco, F., *Contrib. Emb.*, 1942, 30, 129; Hewer, Evelyn, *Jour. Anat.*, 1932, 66, 488; Katznelson, Z. S., *Anat. Rec.*, 1934, 61, 109.
- [2] For stratification of intercostal muscles, see Walmsley, T., *Jour. Anat.*, 1916, 50, 165; Davies, Gladstone and Stibbe, *ibid.*, 1932, 66, 323; Siddiqui and Mullick, *ibid.*, 1935, 69, 350.
- [3] For segmental distribution of nerves in body-wall, see Davies and Others under note [2]; Davies, F., *Jour. Anat.*, 1936, 70, 177.
- [4] Howell, A. B., *Anat. Rec.*, 1936, 66, 295 (phylogeny of muscular system); Winckler, G., *Archiv. d'Anat.*, 1938, 25, 137 (phylogeny of erector spinae).
- [5] Haines, R. Wheeler, *Jour. Anat.*, 1936, 70, 33 (nerve-supply as guide to homology of muscles).
- [6] Broman, I., *Ergeb. d. Anat.*, 1906, 16, 639.
- [7] Kiss, F., *Ann. d'Anat. Path.*, 1933, 10, 1078 (finds three kinds of cells in posterior root ganglia—somatic-sensory, visceral-sensory and visceral-motor); Fisher and Ransom, *Jour. Anat.*, 1934, 68, 1 (a criticism of Kiss's observations); Blair, Bacsich and Davies, *ibid.*, 1936, 70, 1 (confirm observations by Kiss); see

also Kiss, F., *ibid.*, 1932, 66, 488; Sheehan, D., *Anat. Rec.*, 1933, 55, 111 (finds efferent fibres in posterior roots); Hirst, A., *Zeitsch. Anat. Entwickl.*, 1928, 87, 275; Kolosow and Polykarpowa, *Anat. Anz.*, 1935, 80, 239.

[8] Detwiler, S. R., *Anat. Rec.*, 1934, 61, 441; Streeter, G. L., *Jour. Comp. Neur.*, 1933, 57, 455.

[9] Gaskell's first paper on the sympathetic system appeared in *Jour. Physiol.*, 1886, 7, 1; Langley's work will be found in *The Autonomic Nervous System*, 1921. The history of the autonomic system has been traced by Prof. D. Sheehan in *Archiv. Neur. Psych.*, 1936, 35, 1051. Dr. J. Botar proposes to modify Langley's conception in *C.R. l'Assoc. d'Anat.*, 1933, 28. The autonomic system in the Primates is dealt with by Prof. S. Zuckerman, *Trans. Zool. Soc. Lond.*, 1938, 23, 315. Sheehan and Pick, *Jour. Anat.*, 1943, 77, 125 (rami communicantes in the rhesus monkey).

[10] For recent papers on the distribution of white rami, see Delmas, J., *Ann. d'Anat. Path.*, 1933, 10, 1059; Kuntz and Moseley, *Jour. Comp. Neur.*, 1936, 64, 63.

[11] Although the separation of the visceral nerves into three sets—cranial, dorsal and sacral—has received no full explanation, yet it is helpful to remember that in the earliest (water-breathing) vertebrates the cranial system is concerned with the intake of food and air and with their distribution in the body (circulation), while the sacral system is concerned with the output of waste and sex products.

[12] Stopford, Sir J., *Jour. Anat.*, 1929, 63, 285; Telford and Stopford, *ibid.*, 1933, 67, 417; Woollard, H. H., *Brain*, 1935, 58, 352.

[13] See papers by the late Prof. H. H. Woollard and his Associates on distribution of cutaneous nerves, *Jour. Anat.*, 1939, 73, 559; 1940, 74, 413, 429.

[14] Weddell, G., *Jour. Anat.*, 1941, 73, 441; 1943, 77, 49.

connect the sensory with the contractile or muscle cells. Those connected with the sensory cells—the posterior root ganglia—arise at the lateral margins of the medullary plates, those connected with the muscle cells arise near their mesial margins. If this hypothesis is true, then the central canal is merely an enclosed tube of ectoderm and filled with fluid because the form of animal in which the medullary plates were evolved was a water-living form. Gaskell advanced the view that the central canal represents a former alimentary tube round which nerve cells have gathered. While Gaskell's hypothesis explains many facts, it leaves many more unexplained—especially the manner in which the

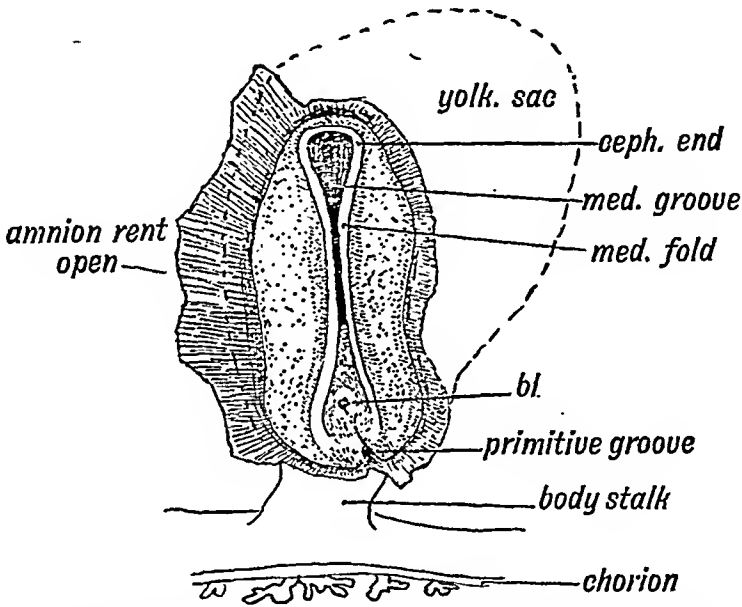


FIG. 90. Medullary Folds uniting to form the Neural Tube in a Human Embryo late in the 3rd week of development. *bl.*, blastopore or neurenteric canal. (After Graf Spee.)

central nervous system is developed. Hence this hypothesis is now abandoned.

Formation of the Central Canal.—The medullary plates of ectoderm, which form the spinal cord and brain, rise up, meet and enclose a canal—the central canal of the spinal cord and brain (Fig. 90). The lips of the medullary plates meet and fuse together in the cervical region first; the process of union spreading forwards and backwards, the last parts to be enclosed being the cephalic and caudal extremities [1]. The opening at the anterior extremity—the *anterior neuropore*—and that at the hinder end—the *posterior neuropore*—close at the middle of the 4th week (20–25 somites), the anterior neuropore closing first. The optic vesicles begin to grow out from the medullary plates before these have united to enclose the cavity of the fore-brain. It will be thus seen that the optic

vesicle, which becomes the retina and optic nerve, is developed as a part of the medullary plate.

Division of the Neural Canal (Figs. 91, 92).—At the end of the 4th week the neural tube is divided into four parts. These are :

(i) An anterior dilatation, the fore-brain, which forms the 3rd and lateral ventricles and their walls. (ii) The mid-brain, which becomes

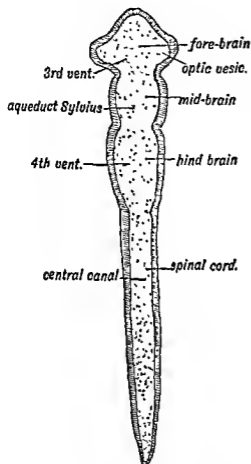


FIG. 91.

FIG. 91. Diagram of the Four Primary Divisions of the Neural Tube.

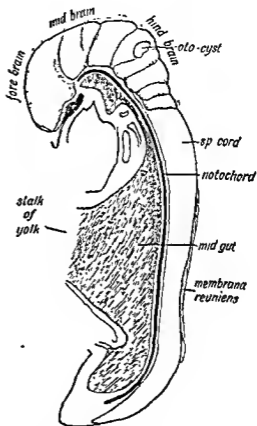


FIG. 92.

FIG. 92. Lateral view of the Central Nervous System of a Human Embryo at the end of the 4th week—2.6 mm long. (Prof Low)

transformed into the aqueduct of Sylvius, corpora quadrigemina and crura cerebri. (iii) The hind-brain, the basis of the 4th ventricle, pons, cerebellum and medulla. (iv) The central canal and spinal cord.

The Spinal Cord.—The spinal cord at first extends throughout the whole length of the spinal column. At the end of the 3rd month the spinal column and canal grow more rapidly than the cord, and at birth its lower end has become withdrawn to the level of the 3rd lumbar vertebra. By the 3rd year it usually terminates opposite the disc

between the 1st and 2nd lumbar vertebrae, but it may stop at the lower border of the 2nd lumbar or rise as high as the middle of the 12th dorsal vertebra [2]. The results of this inequality of growth are:

(i) The roots of the lumbar and sacral nerves become enormously elongated, forming the cauda equina; all the nerves are more or less drawn up, except the 1st and 2nd cervical; the origins of the lower cervical nerves are drawn up 2 vertebrae (as indicated by the position of their spines); the upper dorsal, 3; the lower dorsal, 4; the lower lumbar, 5; the coccygeal, 10. These statistics represent a broad expression of the observations made by the late Prof. R. W. Reid [3].

(ii) The *caudal part* of the spinal cord is the last part of the neural

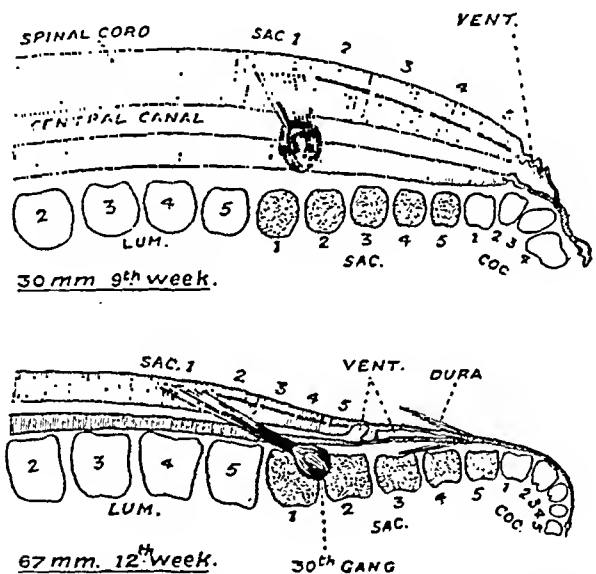


FIG. 93. Showing the differentiation of the terminal part of the Neural Tube into the coccygeal thread and flum terminale. (After Streeter.)

tube to be formed (see Fig. 81, p. 102). Its fate has been investigated by Dr. Streeter [2]. Even in the 9th week (Fig. 93) the caudal segment is still represented over the coccyx, ending in a subcutaneous vesicle, but already retrogression has set in, the coccygeal ganglia have disappeared and the neural canal immediately distal to the origin of the 5th pair of sacral nerves is becoming dilated to form the terminal ventricle [4]. By the 12th week (Fig. 93), when retraction has set in, we see that the caudal segment has become differentiated into a distal or extradural part, which is drawn out to form the coccygeal thread, while the intradural part is being stretched and will become the flum terminale.

Differentiation of the Spinal Cord.—As the neural plate begins to be folded in about the end of the 3rd week, the single layer of columnar epithelium of which it is composed is already undergoing certain changes.

Three stages in its differentiation are shown in Fig. 94; in Stage I, the single layer of ill-defined columnar cells is shown; the bases of the cells are directed towards the central canal, resting on a delicate *internal limiting membrane*; their outer ends, appearing on the surface of the neural tube, are bounded by the *external limiting membrane*. In Stage II there have been an active proliferation of cells and an increase in the thickness of the neural wall; the cell bodies have become elongated and appear to form a cytoplasmic syncytium, in which the nuclei are implanted [5]. In Stage III (Fig. 94), which is reached about the close of the 4th week, the wall has made a further increase in thickness; in the cellular cytoplasm a fibrillar meshwork—a *myelospongium*—has been laid down; three zones can be distinguished, a middle or *mantle zone*

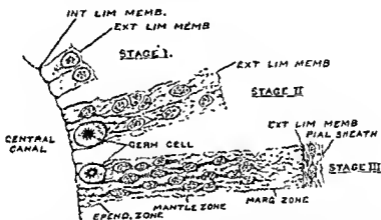


FIG. 94. Three stages in the early differentiation of the wall of the Spinal Neural Tube. Stage I, single layer of ill-differentiated columnar epithelium. Stage II, in which the single layer has been transformed into a nucleated syncytium; Stage III, in which three zones begin to be apparent. (After Streeter)

in which most of the nuclei are contained and which will become the grey substance of the cord; an outer or *marginal zone* made up of myelospongium into which the fibre-tracts of the cord will grow; an inner or *ependymal zone*, not distinctly demarcated, but characterized by the presence of *medulloblasts*—often named *germinal cells*, which contain actively dividing large nuclei. The medulloblasts are becoming differentiated into neuroblasts, the producers of nerve cells, and into neuroglial or supporting cells. Neuroglial fibres are laid down in the cell-protoplasm of neuroglial cells. The ependymal cells, which line the central canal, are derived from medulloblasts of the inner zone.

The *medulloblasts* give origin not only to neuroblasts and supporting or neuroglial cells but also to other cells of a migratory nature. There are, in the first place, *sheath cells*, which pass out with the anterior roots to provide sheaths for nerve fibres; there are, in the second place, three other forms which remain within the central nervous system and are

between the right and left posterior funiculi developing on each side of the original roof plate. In the 11th week the central canal and ependymal zone are further reduced; the posterior-median septum has increased in depth owing to the rapid growth of the posterior funiculi; the middle or mantle zone is now differentiated into the anterior and posterior columns of grey matter. In the 13th week the adult condition is reached; the central canal is reduced to its final size, the ependymal zone now forms merely a lining to the canal; the anterior and posterior horns, with their various groups of nerve cells, are reaching their final form, while in the marginal zone the great connecting and association tracts of white matter have arisen or are arising. There is now a deep posterior-median septum and an open anterior-median fissure, formed during the development of the ventral funiculi in the anterior part of the marginal zone [8].

Spinal Tracts.—With the formation of the posterior columns, the grey matter of the dorsal laminae, at first united by the roof plate, becomes widely separated to form the posterior horns (Fig. 97). At the same time part of the gelatinous tissue of the inner zone is separated to form a cap on the posterior horns (Fig. 96, *B*). In the gelatinous tissue congenital cysts may arise. The columnar cells which line the central canal are ciliated. Thus by the end of the 3rd month the nerve cells have taken up their permanent stations in the grey columns of the spinal cord. The cells that have to do with the reception and transmission of sensory messages are situated in the posterior root ganglia; those that have to do with the dispatch of motor impulses are situated in the anterior and lateral horns; the remainder may be regarded as intercalated or shunt cells, and are concerned in linking up or associating the afferent and efferent systems and centres. The marginal zone provides a basis into which the nerve processes—the axons which are to connect neuron with neuron and centre with centre—may grow and reach their destinations. It is a remarkable fact that the lower we go in the vertebrate scale the more automatic or independent do the nerve centres of the spinal cord become; the higher we go in the scale the more they become dominated by and dependent upon nerve centres situated in the hind-brain, mid-brain and fore-brain. Hence we are prepared to find that the first tracts of nerve fibres which appear in the marginal zone are those which link together the nerve centres in the spinal cord itself. Early in the 2nd month the fibres of the posterior root have entered the marginal zone on the dorsal side of the cord, and have thus formed the rudiment of the posterior funiculi; these effect connections with receptive nuclei in the posterior horns and with the gracile and cuneate nuclei. The posterior funiculi reach their maximal size in the human spinal

cord. Next in point of development of these tracts come anthropoid apes. Fibre-tracts which associate neighbouring or allied nuclei or centres of the cord appear in the marginal zone of the lateral and anterior parts of the cord. These may be described as inter-segmental tracts.

Later, in the 3rd month, commences the growth of fibres within the antero-lateral marginal zone of (i) tracts which, arising from cells in the cord, are to end in hind-brain, mid-brain and fore-brain, and thus supply these higher centres with afferent impulses which are reaching the spinal centres; (ii) tracts which, commencing in the hind- and mid-brain,

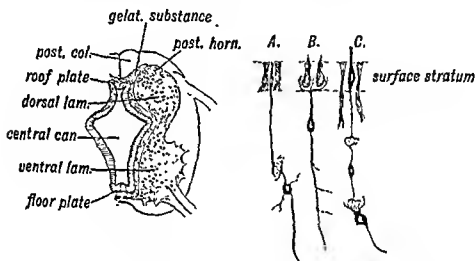


FIG. 97

FIG. 98

Fig. 97 Diagrammatic section of the developing Spinal Cord to show (1) the Roof and floor plates; (2) the dorsal (alar) and ventral (basal) Laminae; (3) the gelatinous tissue between the middle and lower zones.

Fig. 98 Showing transformation of Cells of the Ectoderm to sense epithelium, nerve cells and supporting cells, in A, the olfactory plate; B, the otocyst; C, the retinal layer of optic cup

grow down to permit the higher centres to influence the lower centres in the cord. Lastly, in the 5th month, the pallio-spinal or *pyramidal tracts* commence to develop. The pyramidal tracts (crossed and direct) grow down from the cells of the motor cortex. They are medullated in the 18th month which follows birth, but in thickness medullary sheaths increase until puberty is reached. The pyramidal tracts are the means by which the brain controls the motor cells of the cord. In man these tracts are remarkable not only for their great size, but also that in addition to the crossed lateral tract, which is present in all mammals, there is also an anterior or direct tract. The anterior tract appears to be a recently evolved system; it is extremely variable in size. The only other animals which possess it are the nearest allies of man—the

great anthropoid apes. The great size of the somatic-motor (pyramidal) and of the somatic-sensory (posterior funicular) tract in the human spinal cord is correlated with the extent of the motor and sensory areas of the human brain.

The *myelinization* [9]—the formation of medullary sheaths for the fibres of nerve tracts—commences early in the 4th month and is not really finished until about 18 months after birth. The oldest tracts—the ones which are first required to carry messages—are the earliest to be medullated. The first fibres to be medullated are those of the anterior roots, then follow the posterior roots. By the 8th month all the fundamental tracts of the cord are myelinated, those carrying messages towards the brain preceding those conveying efferent messages. The pyramidal tracts are the last to be ensheathed. The process begins in the oldest part of the fibre—the part nearest the parent nerve cell—and spreads towards the growing tip. The great nerve tracts are ensheathed at different dates; hence it is possible to distinguish and unravel one tract from another during the period of development. The myelin sheath insulates a nerve fibre, conserving and expediting the messages transmitted by it.

Segments of the Spinal Cord.—To that part of the neural tube and neural crest which corresponds in position to a primitive body segment the name of *Neuromere* is given. From the cells of a neuromere are produced the posterior and anterior root of a spinal nerve on each side. The extent of each neuromere is thus marked out by the attachments of its nerve roots. As already explained (p. 110), the segmentation of the spinal cord is secondary to and dependent upon the segmentation of the mesodermal mass which lies on each side of it and which comes to surround it. At no time are the medullary plates divided into embryological segments in the same sense as the mesoderm is divided. Yet the neural tube probably did arise from the fusion of a series of neuromeres or ganglia, each presiding over a definite segment of the body, subsequent evolutionary changes having led to their fusion. Dr. Watt observed in a human embryo in which there were 18 body somites that 11 segments were to be noted in the spinal cord. The cervical and lumbar enlargements of the cord appear in the 4th month. They contain the neuroblasts connected with the body segments which give rise to the buds of the upper and lower extremities. The neuroblasts are arranged not according to the original neural segments but rather in relationship to the movements of the limb. The group representing the hand movements lie behind (distal to) those representing movements of the forearm [10].

Origin of the Medullary Plates and Nerve Cells.—The medullary plates,

like the olfactory plates which give rise to the sense-epithelium of the nose, the otocyst from which the auditory organ is developed, and the retinae, are derived from the ectodermal covering of the embryo [11]. The olfactory plate retains to the greatest extent the features of the ectoderm (Fig. 98, A). Its cells are of three kinds: (i) protective, (ii) secretory, (iii) sensory, the latter being essentially superficial nerve cells. A process or axis cylinder is produced from each sense cell; from its opposite extremity a sensory process is produced. In worms, sense epithelial cells sink beneath the protective and secretory cells, the sensory process being drawn out to form a fibre. In the otocyst, the sensory cells produce no axis-cylinder process, but a ganglionic cell—arising from the ectoderm of the neural crest—comes into connection with it (Fig. 98, B). From the ganglionic cells are produced: (i) a chief process or axis cylinder; (ii) a branching process or processes—*dendrites*—from the opposite pole, which end in an arborescence round the sensory cells. To a nerve cell and all the processes developed from it the name of *Neuron* is given. In the retina, as in the olfactory plate, three types of cells are seen: (i) protective or supporting, which form the fibres of Müller; (ii) secretory, situated over the ciliary processes; (iii) the sensory cells, which produce an axis cylinder on one side and a rod or cone on the other (Fig. 98, C). Further, by a process of division, bipolar and ganglionic cells are produced from the retinal sense cells. In the medullary plates of the spinal cord the representatives of the original ectoderm form the ependymal and neuroglial cells, the first of which may be regarded as both secretory and supporting; the neuroblasts arise by a process of division from the primary ectodermal cells (medulloblasts). A neuron represents a modified neuroblast. The axons or axis cylinders of such neuroblasts are in many cases 2 ft. or more in length; for instance, the motor and sensory fibres which pass from the lumbar enlargement to the muscles and skin of the foot. The nerve cells in the basal laminae are peculiar in that their axis cylinders end on muscle cells.

Malformations of the Neural Canal.—The fact that children are occasionally born with the medullary plates open and exposed on the head and back has already been mentioned (see Fig. 88). *Total rachischisis*, as the condition is named, is rare; it is much more usual to find only one part of the neural tube open: either the anterior or cephalic part, giving the condition known as *anencephaly*, an open condition of the brain; or the posterior or lumbo-sacral part, giving the condition known as *cystic spina bifida*. The latter condition is shown in Fig. 99. As the spinal cord is followed down, it is seen to enter a cystic structure formed by a dilatation of the subarachnoid space, across which the roots

great anthropoid apes. The great size of the somatic-motor (pyramidal) and of the somatic-sensory (posterior-funicular) tract in the human spinal cord is correlated with the extent of the motor and sensory areas of the human brain.

The *myelinization* [9]—the formation of medullary sheaths for the fibres of nerve tracts—commences early in the 4th month and is not really finished until about 18 months after birth. The oldest tracts—the ones which are first required to carry messages—are the earliest to be medullated. The first fibres to be medullated are those of the anterior roots, then follow the posterior roots. By the 8th month all the fundamental tracts of the cord are myelinated, those carrying messages towards the brain preceding those conveying efferent messages. The pyramidal tracts are the last to be ensheathed. The process begins in the oldest part of the fibre—the part nearest the parent nerve cell—and spreads towards the growing tip. The great nerve tracts are ensheathed at different dates; hence it is possible to distinguish and unravel one tract from another during the period of development. The myelin sheath insulates a nerve fibre, conserving and expediting the messages transmitted by it.

Segments of the Spinal Cord.—To that part of the neural tube and neural crest which corresponds in position to a primitive body segment the name of *Neuromere* is given. From the cells of a neuromere are produced the posterior and anterior root of a spinal nerve on each side. The extent of each neuromere is thus marked out by the attachments of its nerve roots. As already explained (p. 110), the segmentation of the spinal cord is secondary to and dependent upon the segmentation of the mesodermal mass which lies on each side of it and which comes to surround it. At no time are the medullary plates divided into embryological segments in the same sense as the mesoderm is divided. Yet the neural tube probably did arise from the fusion of a series of neuromeres or ganglia, each presiding over a definite segment of the body, subsequent evolutionary changes having led to their fusion. Dr. Watt observed in a human embryo in which there were 18 body somites that 11 segments were to be noted in the spinal cord. The cervical and lumbar enlargements of the cord appear in the 4th month. They contain the neuroblasts connected with the body segments which give rise to the buds of the upper and lower extremities. The neuroblasts are arranged not according to the original neural segments but rather in relationship to the movements of the limb. The group representing the hand movements lie behind (distal to) those representing movements of the forearm [10].

Origin of the Medullary Plates and Nerve Cells.—The medullary plates,

layer, and an outer or arachno-dural. The cleft becomes the sub-arachnoid space. Later, during the 5th month, the arachnoid membrane becomes separated from the dura (Spirow).

Development of Nerves [14].—The belief, at one time widely held, that nerve fibres arise by the union of a chain of cells has been given up. Everyone now accepts the theory promulgated by His and by Koelliker in the latter part of the 19th century, that no matter how long a fibre may be, it represents an outgrowth from a single embryonic nerve cell or neuroblast. Prof. His based his belief on the appearance presented by the anterior and posterior nerve roots at their first appearance in the embryo. The processes forming the fibres of the anterior root "seemed" to grow from the cells of the anterior horn of the cord, and those of the

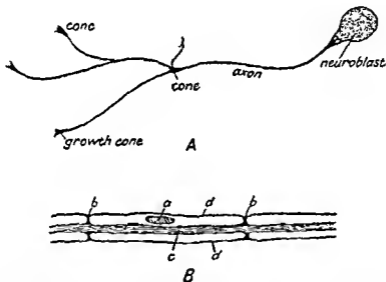


FIG. 100.

- A. Neuroblast with its developing process or axon giving off collateral branches, all of which end in "growth-cones" (After R. G. Harrison)
 B. Section along a Medullated Nerve Fibre showing, a, a sheath cell (of Schwann); b, node of Ranvier; c, axon or axis cylinder; d, neurilemma

posterior root from the ganglionic cells. The first man to see nerve fibres actually sprouting from these cells was Dr. Ross G. Harrison, of Yale. In 1908, having succeeded in keeping part of the spinal cord of a tadpole alive in a lymph medium, he noted, through his microscope, the actual growth of the processes; they grew at a rate of a micron a minute.

In Fig. 100 a growing nerve fibre is depicted, with the neuroblast by which it is being produced. The fibre or process has given off branches; each branch, as well as the main or original process, ends in a "growth-cone." A growth-cone behaves almost as if it were a sentient thing: when it encounters obstacles it attempts to circumvent them. The

of the lumbo-sacral nerves pass. The projecting dome of the cyst is formed by the expanded medullary plates; hence the spinal cord appears to end on the wall of the cyst and spinal nerves to actually arise from it. The lumbo-sacral parts of the neural tube and of the spine have never been enclosed; the cerebro-spinal fluid collects in the subarachnoid space, and the unresisting medullary plates are raised up to form part of the wall of a cystic tumour. Another form of pathological dilatation may appear after the neural tube is completely closed. In chicks hatched at abnormal temperatures fluid may collect in certain parts of the tube, thus dilating it and giving rise to cystic conditions [12].

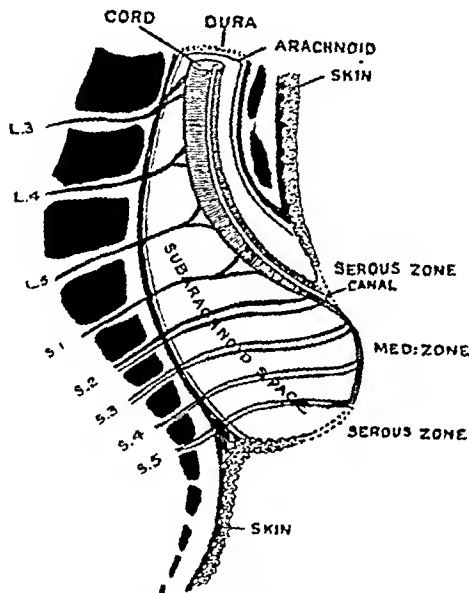


FIG. 90. Vertical section of the Lumbar Region to show the arrangement of parts in a typical case of cystic spina bifida.

Membranes and Vessels of the Cord.—As the neural tube is being enclosed during the 4th week by the upgrowth of mesoderm in the medullary folds, mesenchymal cells become applied to the neural tube. They form the primary sheath of the neural tube (Fig. 94). In lower vertebrates the neural crest contributes to the formation of this membrane; this is probably also the case in higher vertebrates, including man. The pigment cells of the pia mater are so derived. Thus the cord and central nervous system have a wrapping of ectodermal origin [13]. The ensheathing tissue of the cord receives a vascular supply from each dorsal branch of the segmental arteries and veins. Branches of these vessels perforate the nerve tissue, and thus a vascular mesodermal element is added. By the middle of the 2nd month the tissue forming the primary sheath of the cord has become cleft into an inner or pial

CHAPTER IX

THE MID- AND HIND-BRAINS

When the neural tube is traced forwards into the head region, it is seen to undergo a marked change in form—a transformation due to a change in function. In the spinal cord the nerves arise in two rows—a dorsal sensory and a ventral motor; here the dorsal and ventral series are still represented, but a third or intermediate series has been added. This third series is represented by the spinal accessory (XI), vagus (X) and glossopharyngeal (IX), facial (VII) and fifth (V) pairs of nerves. They arise from intermediate columns of cells representing in an exaggerated degree the splanchnic or visceral nerve columns of the spinal cord. Further, the central canal becomes enlarged to form the 4th ventricle. The hinder part of the roof of the 4th ventricle becomes reduced to a membranous lamina, forming the medullary velum and choroid plexus—a secretory mechanism—while the front part of the roof becomes the seat of a complex mechanism (the cerebellum) for the coordination of impulses dispatched to motor centres in the spinal cord and brain stem. This high degree of specialization almost obliterates the original simple nature of that part of the neural tube which forms the mid- and hind-brain. Further, the neural tube in the regions of the mid- and hind-brain, as in the spinal cord, lies over the notochord (Fig. 101). The notochord ceases at the junction of the mid- and fore-brain. The developing walls of the mid- and hind-brain show the same three zones as were seen in the spinal cord—inner or ependymal, middle or mantle and outer or marginal. We shall find, too, the same division of each lateral neural plate into basal and alar laminae.

A reference to the relationships of the hind-brain during the 4th week of development (Fig. 101) serves to explain why the vital centres of the body—those which are concerned in the regulation of respiration, circulation, deglutition and digestion—come to be placed in its walls. At this time the hind-brain lies over the pharynx, with its aortic arches and its gill-pockets—representing the breathing mechanism of fishes. When lungs arise the control of respiration still lies in the original respiratory centres of the hind-brain. The heart too lies directly under, or ventral to, the hind-brain (Fig. 101); hence the centres for circulation are placed there. The fore-gut, from which the mouth, pharynx, oesophagus, trachea, lungs, stomach and liver are to arise, is

R. G., *Anat. Anz.*, 1938, 85, 3 (suppl.); Spirow, M., *Archiv. Russ. Anat. Hist. Emb.*, 1933, 12, 229.

[14] Concerning the development of nerve fibres, see Speidel, C. C., *Jour. Exper. Zool.*, 1932, 61, 279; *Amer. Jour. Anat.*, 1933, 51, 1. For the part played by sheath cells in nerve repair, see Glees, P., *Jour. Anat.*, 1943, 77, 153. Dr. R. G. Harrison summarized our knowledge concerning the development of nerve fibres in his Croonian Lecture to the Royal Society in 1935 (*Proc. Roy. Soc.*, 1935, 118 (B), 155).

[15] For origin of sheath cells, see Raven, C. P., *Jour. Comp. Neur.*, 1937, 67, 321; see also references to Harrison and to Detwiler in note [13].

[16] For literature on the independency of neurons, see Woollard, H. H., *Jour. Anat.*, 1937, 71, 480; Woollard and Harpman, *ibid.*, 1939, 73, 361; Young, J. Z., *Phil. Trans.*, 1939, 229, 465; Stoeher, P., *Zeitsch. Anat. Entwickl.*, 1935, 104, 133; Boeke, P., *Anat. Anz.*, 1938, 85, 111 (suppl.); Nonidez, J. F., *ibid.*, 1937, 84, 1, 315.

produced; a middle or mantle zone, in which neuroblasts, neurological fibres and young nerve fibres are being differentiated; and an outer or marginal zone. By the 6th week the disposition of the nuclei connected with the cranial nerves in the mantle zone can be made out. The

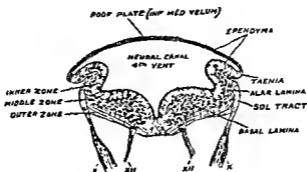


FIG. 102 Section across the Hind-Brain of a Human Embryo in the 6th week.

grouping of the nuclei as seen in a diagrammatic section across the hind-brain is shown in Fig. 103. In the mantle zone of the basal lamina are three columns of motor cells—the columns being much interrupted as they are traced from the lower to the upper end of the hind-brain. These

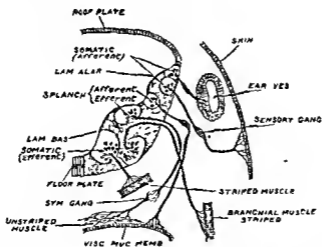


FIG. 103 Diagrammatic section across the Hind-Brain to show the grouping of cranial nerves and their nuclei. (After Elliot Smith)

are: (i) the *somatic motor*, continuing upwards the somatic cells of the anterior horn and supplying muscles derived from the body somites; from this column arise the XIIth and VIth nerves. (ii) The *lateral somatic motor*, supplying striped muscles which were first evolved for the movement of gill-arches; from this column arise motor fibres of XI, X, IX, VII and V. The nucleus ambiguus forms part of this column. (iii) The *splanchnic motor* nuclei, giving origin to fibres

also placed in the territory of the hind-brain. Its relationship to the otocyst, however, is to prove the most important. From that structure is to arise a vestibular or balancing mechanism designed to supply information concerning the position and movements of the head. The cerebellum, the development of which so transforms the simple tubular hind-brain, arises in connection with the vestibular nuclei. One other point may be noted before proceeding to follow the transformation of the hind-brain into medulla oblongata, cerebellum and pons. The hind-brain is interpolated between the spinal cord on the one hand and the mid- and fore-brain on the other; hence it becomes the great highway for the nerve tracts which are developed to link brain and spinal cord.

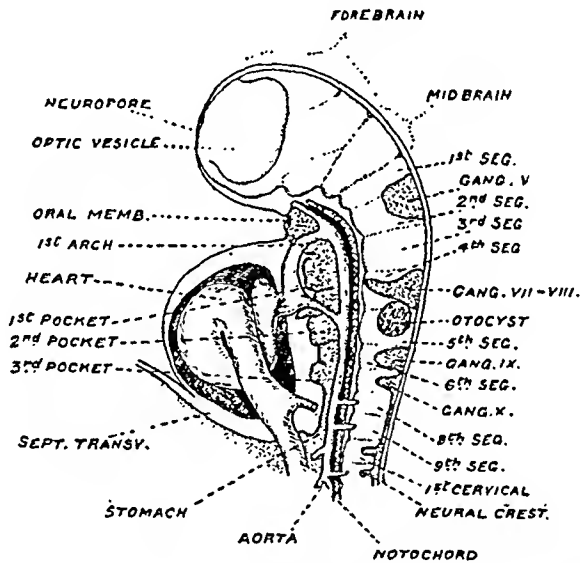


FIG. 101. Showing the tubular form, the neuromeres and relations of the Mid- and Hind-Brain in a Human Embryo in which there were 18 body somites—in the 4th week of development. Nine segments or neuromeres are depicted in the hind-brain of this embryo; this is exceptional; the usual number is seven. (After Crawford Watt.)

into a functional whole. Throughout the greater part of the 2nd month the hind-brain forms only a little less than half of the total length of the neural tube.

4th Ventricle.—The cavity or neural canal of the hind-brain becomes the 4th ventricle. In its floor are developed, out of the *basal* or *ventral* and *alar* or *dorsal laminae* (Fig. 102) of the neural plates, the pons and medulla. In its roof are developed the cerebellum, the superior and inferior medullary vela [1].

Basal and Alar Laminae of the Medulla.—The basal and alar laminae of the neural tube become flattened out to form the floor of the hind-brain. At the end of the 4th week each medullary plate shows on section three zones: an inner or ependymal, where new cells are being

struck by the power of neuroblasts to migrate—particularly those which make up the nuclei of motor nerves; they were drawn towards the terminal nuclei from which they received their chief incoming stimuli or messages.

For example he noted a forward movement of the motor nucleus of the XIIth towards the receptive nuclei of the IXth and Xth; of the VIIth towards the descending root of the Vth, while the nuclei of the XIth for the sternomastoid and trapezius tend to spread backwards in the spinal cord towards the receptive nuclei of the neck and shoulder. To the law or force which regulates the mass-movement or migration of neuroblasts Kappers gave the name *Neurobiotaxis*. We have just

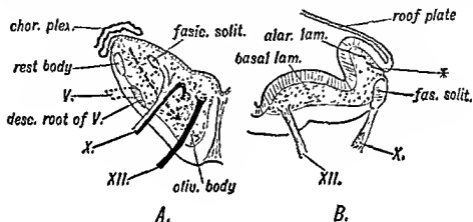


FIG. 101.

B. The Alar and Basal Laminæ of the Hind-Brain at the beginning of the 6th week to show the superficial position of the sensory root of the Vagus. (Compare with A.) The rhombic lip and the point at which the root of the Vth nerve and restiform body will be formed is indicated by an asterisk (After His.)

mentioned the migrations which give rise to the olivary bodies of the medulla, but we shall find as we ascend the brain stem—to cerebellum and pons, to mid-brain and basal ganglia and particularly to the cerebrum itself—that neuroblastic migration is a basal principle of development and transforms the simple embryonic neural tube into the complexities of the adult brain. In the spinal cord neuroblasts are confined to the mantle zone, but in the hind-, mid- and fore-brains they invade the marginal zone and there establish their chief centres. The cortex of the cerebellum and cerebrum are produced by a neuroblastic invasion of the marginal zone. Nor is the mass-migration of nerve cells really different from other manifestations of living cells. Outgrowing processes from the neuroblasts of the spinal ganglia and spinal cord spread into the limb-buds and reach their destinations unerringly—drawn and

distributed to the musculature of the heart, lungs and alimentary canal—represented by the dorsal nuclei of IX, X, XI and the salivatory nucleus of the VIIth. In the alar lamina are differentiated two main groups or columns of sensory or reception nuclei: (i) *splanchnic*, which receive the ingrowing fibres of the VIIth–IXth–Xth nerves—and therefore are in connection with the pharynx, heart, lungs and alimentary canal, receiving afferent impulses from all, including those of taste; (ii) *somatic*, corresponding to the posterior horn cells of the spinal cord and receiving fibres in series with the posterior roots of spinal nerves. The posterior root fibres in the cranial series are represented by the sensory root of the Vth and by the VIIIth nerve—both vestibular and cochlear divisions. The VIIIth nerve and its ganglia were probably derived from the same system as gave rise to the complex sensory organs of the lateral line of fishes, and should be distinguished from the ordinary somatic group.

We have seen how the posterior funiculi are formed in the marginal zone of the spinal cord by fibres of the posterior roots. The sensory fibres of the cranial nerves also form tracts in the marginal zone; the solitary tract is formed by fibres of the IXth and also of the Xth and VIIth. The vestibular and Vth nerves also form tracts—the latter being particularly extensive, extending down the spinal cord to the level of the 4th cervical nerve. At first these tracts lie near the surface of the hind-brain, but in the 6th week they become overwhelmed and buried by vast migrations of neuroblasts.

Neurobiotaxis.—In Fig. 104, *B*, is given a diagrammatic section across the right half of the neural plate of the hind-brain at the 6th week of development, showing the solitary tract in the marginal zone of the ventral surface; in Fig. 104, *A*, is given the condition in the 8th week, showing the fasciculus solitarius buried deeply—much nearer to the dorsal than to the ventral aspect of the medulla. What has happened is this; swarms of neuroblasts have been produced in the ependymal zone near the dorsal margin of the alar lamina at the rhombic lip marked by an asterisk in Fig. 104, *B*. In the spinal cord neuroblastic production goes on longer in the posterior than in the anterior horn; in the hind-brain this tendency to the production of neuroblasts in the dorsal margin of the alar lamina has become enormously heightened [2]. The arrow in Fig. 104, *A*, shows the direction of the swarm; they invade the marginal zone, burying the solitary tract, and group themselves, as they approach the floor plate in the middle line, to form the inferior olivary body; the superior olivary body and the great terminal or receptive nuclei—the gracile and cuneate nuclei—are formed in the same way. Dr. Ariens Kappers in his studies on the medulla in 1907 was

recess and subsequently over its entire surface. In the 3rd month cerebro-spinal fluid is being formed—first as a filtrate, later as a true secretion [4]. The fluid percolates through the velum at three places—middle of the roof and at the lateral angles. At first the thin middle area bulges outwards behind the cerebellum; about the end of the 3rd month medial and lateral foramina appear, forming the foramen of Majendie and the openings of the lateral recess at the points of percolation. The subarachnoid spaces begin to form at the sites of escape and from there extend [5].

As shown in Fig. 111, the velum is continuous with the cerebellum

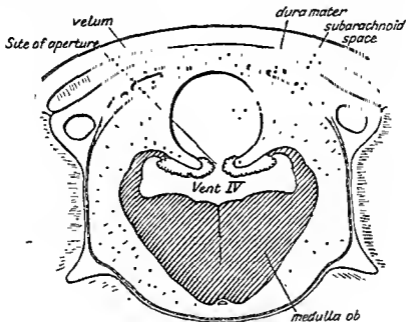


FIG.

J. T. Wilson.)

above and the roof of the central canal of the cord below. In the posterior margin of the cerebellar plates are developed: (i) the nodule; (ii) the flocculus; (iii) the peduncle of the flocculus between (i) and (ii) (Figs. 110, 112). Hence the inferior velum ends above in these structures. The obex and ligula, thickenings or ridges found on the margins of the 4th ventricle, mark the attachment of the roof plate or velum to the rhombic lip of the medullary plates. They represent the attached margin of the velum. The velum is also attached to the restiform body which is developed in the upper margin of the alar lamina. Over the opening of the central canal of the spinal cord into the 4th ventricle there is often a fold formed by the union of the alar laminae [6].

regulated by some obscure force ; Dr. Ross Harrison found that if a limb-bud was transplanted, the nerve fibres which entered it were attracted and moulded to produce a normal supply by some influence in the tissues of the bud. The force which attracts the wandering defensive cells of the body to a site of infection is probably of the same nature as that which regulates the migration of neuroblasts [3].

Inferior Medullary Velum [1].—When a section is made across the hind-brain of an embryo in the 6th week of development, the same parts are seen as in the spinal cord, except that the roof plate has become enormously expanded to form the inferior medullary velum. The extent, shape and attachments of the roof plate are shown in Fig. 105 ; it is diamond-shaped, its hind angle being continuous with the roof plate

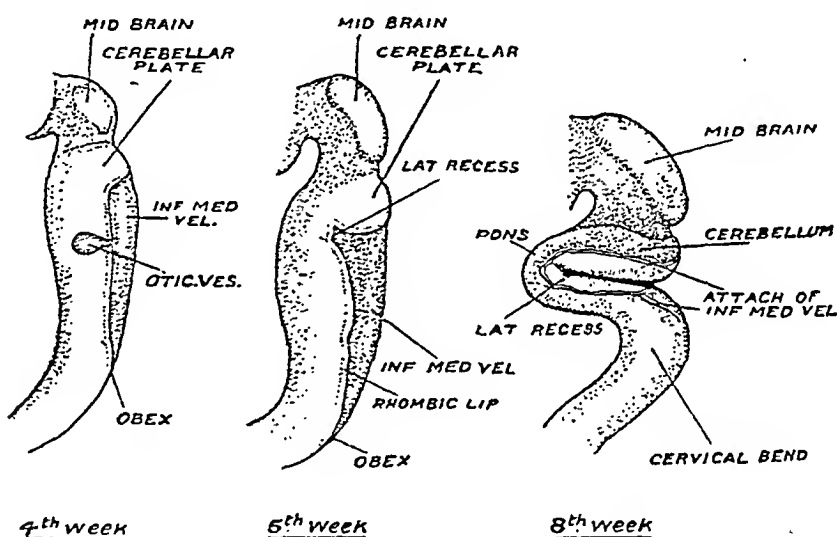


FIG. 105. Showing the origin of the Inferior Medullary Velum from the roof plate of the Hind-Brain.

of the spinal cord, its front angle with the roof plate of the mid-brain, while its lateral angles mark the sites of the two lateral recesses of the 4th ventricle. Its upper margins are attached to the border of that part of the alar lamina which is to produce the cerebellum ; its lower margins are attached to the *rhombic lip*, the dorsal border of the medullary part of the alar lamina. This border is folded outwards (Fig. 102). The shape of the roof plate, or inferior medullary velum, is altered by remarkable changes which set in during the 6th week (Fig. 105) ; growth changes cause the hind-brain to be folded, producing the pontine bend and bringing the cerebellar part of the hind-brain against the medullary. The inferior medullary velum becomes drawn out transversely. A little later—about the 8th week—choroidal villi are produced on its ventricular surface, first in a transverse row extending from lateral recess to lateral

the human cerebellum is very similar in structure to that of a lizard [9]. By this time (Fig. 109) there has been an active proliferation of neuroblasts in the cerebellar plates; they fuse in the middle line to form the vermis or median lobe, and now hulse into the 4th ventricle, much as they do in the frog. What has happened may be best gathered from Fig. 109. The reception nuclei for the VIIIth nerve are developed in the rhombic lip, near the lateral recess; through the vestibular fibres of the VIIIth nerve certain of these nuclei will receive impulses which make them the chief recipients of messages needed for the co-ordination of muscles. The cerebellum is, in the main, a product of the vestibular nuclei. Hence the proliferation of neuroblasts at the rhombic lip and their spread into the cerebellar plates. In the 3rd month neuroblasts

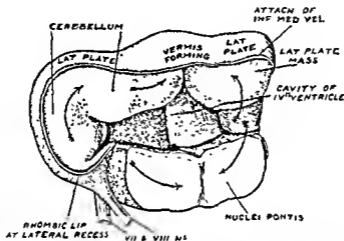


Fig. 109. The Human Cerebellum at the end of the 20th month of development. (After Streeter.) The arrows show the direction of the migration of the pontine and cerebellar nuclei.

invade the marginal zone of the plates and lay the basis of the molecular layer of the cortex. They subsequently retreat to the granular stratum, leaving their main processes in the marginal or molecular zone. The cells of Purkinje—although not fully differentiated until after birth—take up their stations at the junction of the mantle and marginal zones, between the superficial molecular and the deeper granular layers. The axons of the Purkinje cells are the efferent paths of the cerebellar cortex; many end in the nucleus dentatus.

In the 3rd month, when the cerebellar plates are being invaded by cortical elements, other cells, arising in the rhombic lip, invade the adjacent basal laminae—the parts which will become the pons (Fig. 109). There they lie in the path of fibres descending from the frontal cortex, and thus, when they have effected connections with the cerebellum through the fibres of the pons and middle peduncles, bring the cortex of

The velum is to be regarded as a part of the neural tube specially modified for the purpose of secreting the cerebro-spinal fluid that fills the central canal and subarachnoid system. This fluid may help to support the central nervous mass in a mechanical sense, but its rapid

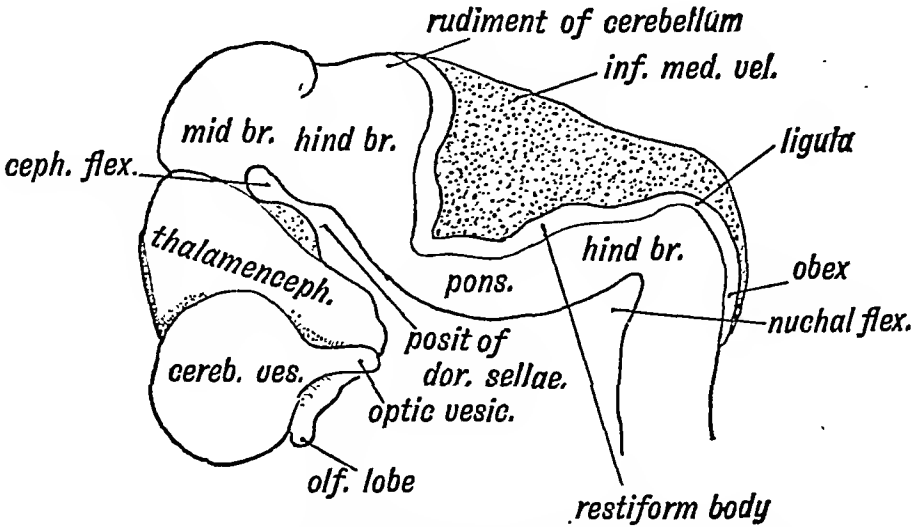


FIG. 107. Lateral view of the Cephalic Part of the Neural Tube in a 5th-week Human Embryo. (After His.)

secretion, its circulation and chemical composition point to some more important nutritive or regulatory influence on the neural centres. It is secreted by the ependymal (ectodermal) epithelium which clothes the choroidal villi [7].

Cerebellum [8].—At the beginning of the 2nd month the cerebellum is

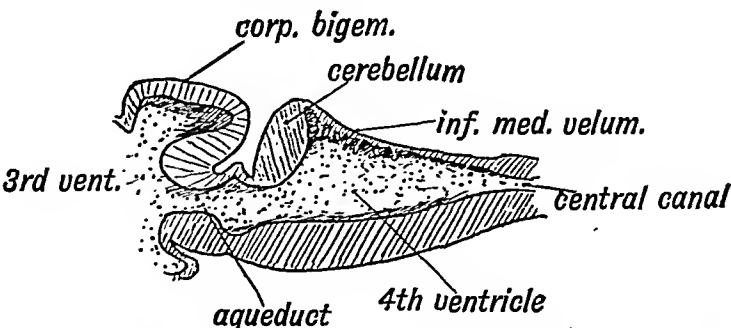


FIG. 108. Median Section of the Cerebellum and 4th Ventricle of a Frog.

still represented by simple right and left alar plates (Figs. 107 and 115), which show the usual triple stratification—an internal proliferating ependymal zone, a middle neuroblastic and an outer marginal meshwork. In the frog a plate-like cerebellum is retained (Fig. 108), for the amphibia have but an imperfect power for sustained co-ordination of their limbs during locomotion on land. At the end of the 2nd month of development

distinguished from the middle lobe, the latest in point of evolution, which may be distinguished as the *neo-cerebellum*. The latter is demarcated anteriorly by the *fissura prima* and posteriorly by the *prae-pyramidal fissure*. The prominence of the pons, the cortex of the *neo-cerebellum*, and that of the *cerebrum* have been correlated in their evolution; cerebellar cortex is linked to cerebral cortex through centres situated in the pons.

Dr. Ahhie [8] found striking evidence of these cortical-pontine connections in his studies of the brains of Australian mammals. In the *Monotremes* there is no frontal cortex and no fronto-pontine tract; transverse fibres are lacking in the upper or anterior half of the pons; the median part of the *neo-cerebellum* is poorly developed. On the other hand, the temporo-pontine tract is well developed; the lower or hinder transverse fibres of the pons are prominent; the median part of the *anterior lobe* is of full size. In the *Marsupial* brain matters are reversed: the frontal cortex and fronto-pontine tracts are present, while the temporo-pontine are missing, with the result that it is the upper part of the pons and the median area of the *neo-cerebellum* which are well developed.

Development of Lobes.—At the end of the 3rd month (Fig. 111) the

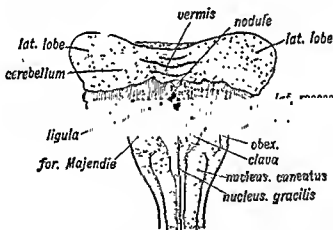


FIG. 111. Diagram of the Cerebellum and of the Attachments of the Inferior Medullary Velum at the end of the 3rd month of development. (After Kollmann)

cerebellum has assumed a dumb-bell form—the lateral elevations representing the right and left hemispheres, which are united by a median plate—the vermis. The cortex has already commenced to expand, as may be seen by the early appearance of transverse fissures on the vermis. It is at this period that the cerebellar plate becomes demarcated into *anterior, middle, posterior, and floccular lobes*, the *fissura prima*, separating the middle from the anterior lobe, appearing very early. Since these

that organ into touch with the cerebrum. The restiform body begins to form in the 2nd month, and by this means the cerebellum is placed in connection with the recipient nuclei of the cord and medulla. The dentate and other central cerebellar nuclei are detached from the invading mass of neuroblasts, the dentate nuclei becoming linked with the red nuclei of the mid-brain by the superior peduncles. In the differentiation of the cerebellum are to be seen numerous illustrations of the law of neurobiotaxis enunciated by Kappers.

Division into Lobes.—Before describing the development of the

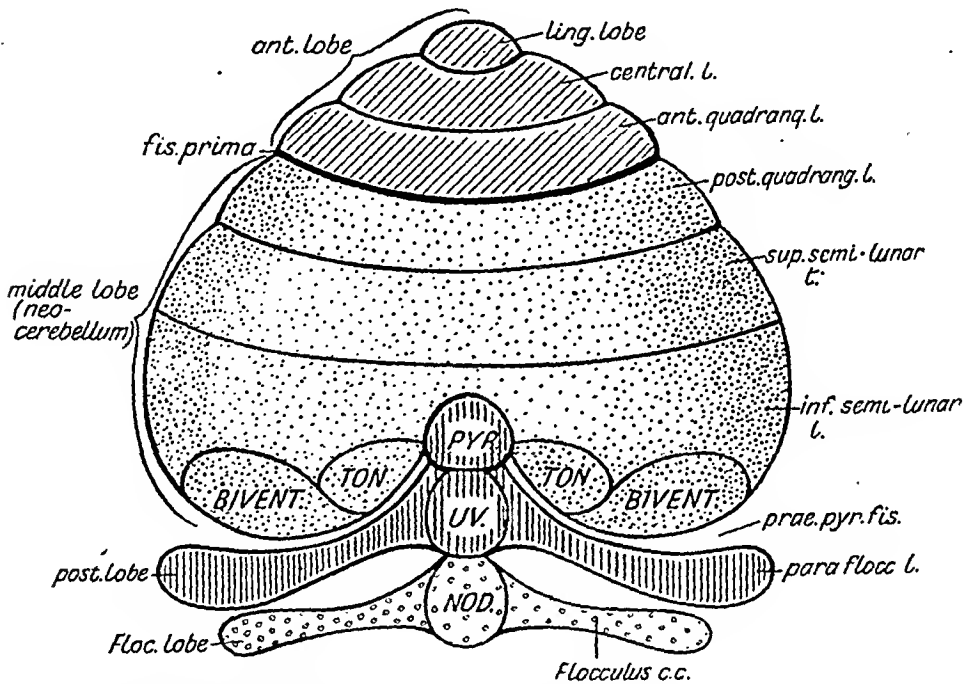


FIG. 110. A diagrammatic representation of the Lobulation of the Cerebellum of the Rhesus Monkey, both upper and lower surfaces being shown. (After Botterell and Fulton.)

NOD., nodule, median element of the floccular lobe; *PYP.*, pyramid; *UV.*, uvula, both being median elements of the parafloccular or posterior lobe; *TON.*, tonsil; *BIVENT.*, biventral, both being parts of the middle cerebellar lobe.

cerebellum, it will be well to note some of the conclusions reached by comparative neurologists as to the division of the organ into lobes. In Fig. 110 is given a diagrammatic representation of the lobulation of a primate cerebellum—that of a rhesus monkey. Both upper and lower surfaces are depicted. The hinder (the most caudal) part, the floccular lobe, is to be distinguished from the rest of the organ. It is closely linked with the vestibular nuclei and is the oldest part of the cerebellum. The rest of the organ is divisible into three lobes—anterior, middle and posterior cerebellar. The anterior and posterior lobes, shaded in Fig. 110, are the older parts and may be called the paleo-cerebellum, as

declive, while the lateral parts are formed by the posterior crescentic (quadrangular) lobuli (Fig. 110). Comparative anatomists speak of the semilunar or crescentic lobuli (Fig. 110) as the *lobulus simplex*. The remaining parts of the middle lobe are the last to be demarcated and developed (5th, 6th months). As these parts of the neo-cerebellum arise there appears between the upper and lower semilunar areas (Fig. 110) the great horizontal fissure (Fig. 113, A), a comparative late feature to appear in the evolution of the primate cerebellum. The cortex of the cerebellum has a uniform structure in all of its lobuli, yet there is evidence of some degree of localization of function [10].

The *Superior Medullary Velum* is part of the roof plate of the 4th

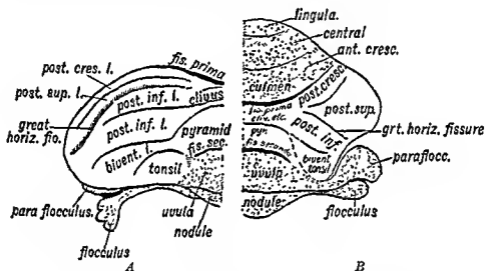


FIG. 113.

- A. Left half of the Cerebellum of a Foetus of 5 months, seen on its inferior aspect. Only the middle, posterior and floccular lobes are exposed. The parts forming the posterior lobe are stippled. (After Elliot Smith) As is mentioned in the text, the pyramid is now assigned to the posterior lobe.
- B. Right half of a typical Mammalian Cerebellum, spread out so as to show the anterior, middle, posterior and floccular lobes. The anterior and posterior lobes are stippled. The fissures and parts are indicated by the terms used in human anatomy in order that the peculiar features of the human cerebellum may be made evident. (After Elliot Smith) Alternative terms used by certain anatomists are given in the text.

ventricle which remains between the superior peduncles. The vestigial lamina which cover it form the lingula.

Three points in connection with the development and comparative anatomy of the cerebellum are especially worthy of attention :

- (i) It arises from the alar laminae, which are directly connected with afferent or sensory nerves only.
- (ii) The part of the neural tube from which the cerebellum arises is the vestibular neuromere—the one to which the internal ear becomes closely linked.
- (iii) The cerebellum reaches its highest development in primates

primary divisions are to be recognized in nearly all mammalian cerebella, they must be of fundamental importance. At the end of the 4th month four fissures are seen to be developed in the human cerebellum (Fig. 112). The rapid growth of the cerebellum, with the pressure of the cerebrum above or in front and the resistance of the occipital bone below or behind, cause the plate-like form to be replaced by one which is wedge-shaped in section, with an upper and lower surface. The minor sulci and fissures of the cerebellum appear between the 5th and 7th months of foetal life.

The floccular lobe is made up of the flocculus on each side with a median element, the nodule, the three parts being united by the pedunculi flocculi (Fig. 110). The floccular lobe is the first to be demarcated in the human foetus. It is separated from the rest of the

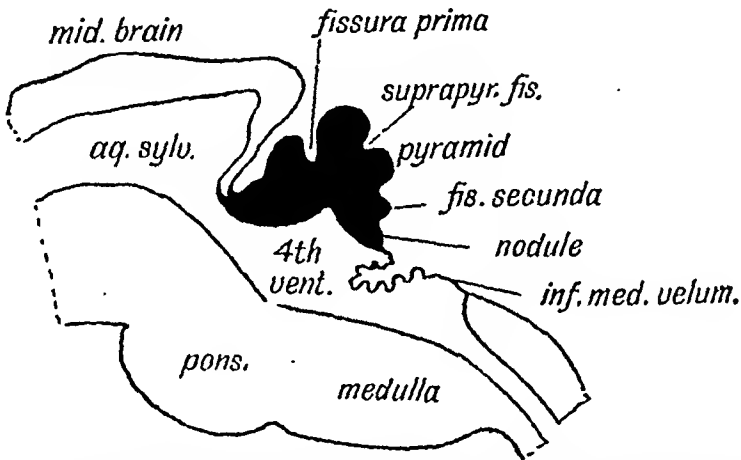


FIG. 112. Diagrammatic Section of the Cerebellum of a Human Foetus early in the 4th month, showing the folding of the cerebellar plate. (After Kuithan and Elliot Smith.)

cerebellum by the prae-nodular fissure. Early to be demarcated, too, is the posterior or parafloccular lobe, with its two median elevations—the pyramid and the uvula. As will be seen from Fig. 113, the late Sir G. Elliot-Smith assigned the pyramid to the middle lobe (neocerebellum), but further research has placed it in the older parafloccular lobe. The fissura secunda (Fig. 113), between the pyramid and uvula, is of minor moment; the more important is the prae-pyramidal which separates the parafloccular from the middle lobe. The paraflocculus (Fig. 113), part of which fills the subarcuate fossa of the petrous bone in lower primates (p. 336), is reduced to a vestige in man and anthropoids.

The various parts of the anterior lobe are demarcated early in development. In Fig. 113, *B*, they are named the lingula, central lobule and anterior crescentic or quadrangular lobule. The culmen is the median part of the last-named lobule. That part of the middle lobe immediately behind the fissura prima appears early. Its median element forms the

anterior limit of the primitive neural tube; it lies over the terminal cephalic part of the notochord (Fig. 101); two cranial nerves (IIIrd and IVth), corresponding to the anterior roots of spinal nerves, arise from it. A section across the mid-brain in the 4th week of development reveals the same divisions as in the cord—lateral neural plates made up of basal and alar laminae, united by a roof plate and a floor plate [11]. The same three zones arise—ependymal, mantle and marginal. In the 3rd month the quadrigeminal plate or *tectum* develops on the dorsal part of its alar laminae, much in the same way as the cerebellum arises within the alar laminae of the hind-brain. Neuroblasts invade the dorsal marginal zone and evolve into a formation which may be described as a cortex.

The quadrigeminal or tectal plate, which arises in the roof-plate of the mid-brain, represents the higher centres or "brain" of cold-blooded vertebrates [12]. Into it there still stream stimuli from the body, from the ear and from the eye. In earlier stages of mammalian evolution this was the executive centre for higher reflex movements of body and limbs. In the course of human development we see the tectum become divided into the two superior colliculi, in which certain optic fibres end, and the inferior colliculi, to which fibres from the cochlear and vestibular nuclei make their way along the lateral lemniscus. The termination of certain optic fibres in the superior colliculus and the origin of the IIIrd and IVth nerves from nuclei in the floor of the aqueduct show how directly the mid-brain serves in the reflexes connected with sight. Just under the tectum is the sensory nucleus of the Vth nerve which gives origin to the ophthalmic division of the Vth nerve. At a very early stage, too, appears, below the floor of the aqueduct and 4th ventricle, the medial longitudinal bundle whose fibres link the motor ocular nuclei with the vestibular nuclei. Associated with the precocious development and myelination of the median longitudinal bundle or fasciculus is the early development of the posterior commissure in the roof-plate of the mid-brain [13].

If the mid-brain is connected with sight it is also the seat of the right and left *Red Nuclei*, which are so closely concerned in the maintenance of posture. These important centres, however, are not entirely situated in the mid-brain; their anterior and more recently evolved parts project into the thalamencephalon.

From the 3rd month of development onwards the mid-brain becomes the highway of developing efferent nerve paths which unite the basal masses and cortex of the fore-brain with nuclei in the pons, medulla and spinal cord, and of afferent or sensory paths which connect the nuclei of the cord, medulla and cerebellum with the basal masses of the

amongst mammals; it is also greatly developed in swimming vertebrates. In primates, as in swimming mammals, the equilibrium of the body is finely and intricately adjusted. On embryological grounds alone we would infer that the cerebellum is part of a sensory or receptor mechanism. Clinical and experimental observations indicate that its main function is to co-ordinate the various muscles of the body in performing definite acts. It is therefore on the afferent nerve system arising from the muscles, joints and bones that the cerebellum has been developed, but its position was determined by the nuclei of the vestibular nerves, cells of which invade the embryonic cerebellar plate.

MID-BRAIN OR MESENCEPHALON

Even in the 7th week of development the mid-brain lies exposed under

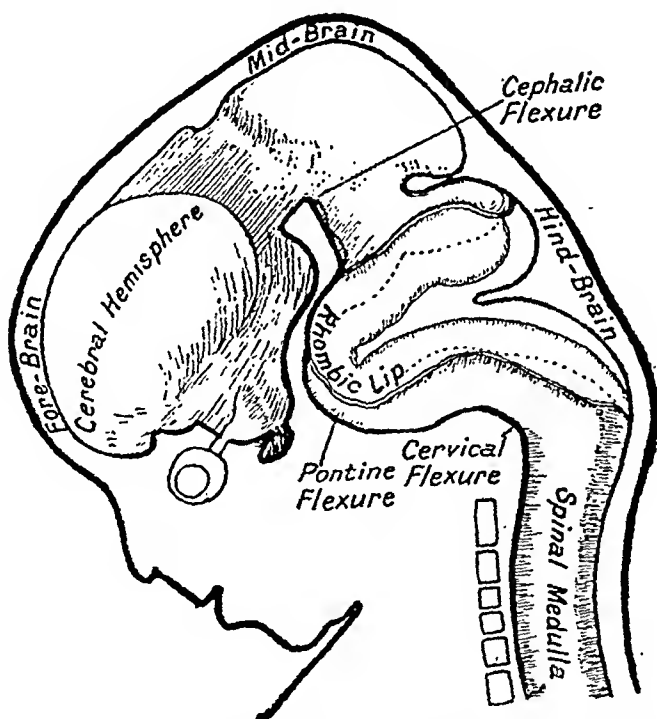


FIG. 114. Sagittal Section of the Head of a Human Foetus in the 7th week of development to show the relationship of the mid-Brain. (Hls.)

the crown of the head (Fig. 114). It is separated from the hind-brain by a constriction—the *isthmus*; in its concavity lies the cephalic flexure (Fig. 114). By the end of the 3rd month it is becoming overshadowed by the preponderating growth of the fore- and hind-brains, and by the 6th month is reduced to the peduncular body which unite cerebrum with cerebellum, its ventricle or canal becoming reduced to the aqueduct which unites the 4th ventricle to the 3rd. When the mid-brain reaches the

manifests its long evolutionary history. In the frog (Fig. 108) the tectal plate is distended by a diverticulum or recess—the *mesocoeliac recess*—of the central canal. Prof. Lucas Keene observed that this recess appears during human development, begins to be filled in during mid-foetal life and is obliterated soon after birth [15].

Constitution of the Mid- and Hind-Brain.—We have traced the development of the neural tube in a forward direction, and have reached the point where the mid-brain passes into the fore-brain. On the roof the point of transition is marked by the posterior commissure (Fig. 115); below the floor the notochord ends (Fig. 101). We have reached the end of the neural tube proper; the part in front—the fore-brain—appears

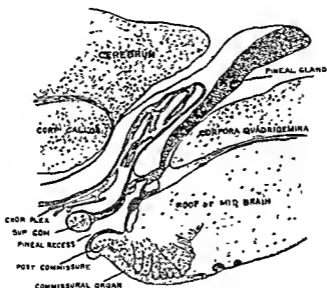


FIG. 115. Section of the anterior part of the Roof of the Mid-Brain of a Cat, to show the subcommissural (commissural) organ. (Dendy and Nicholls)

to have arisen in connection with two great organs of sense, the nose and eye, but we shall also find it to be the seat of centres which dominate the sympathetic system. We find that the neural tube when it enters the region of the head becomes greatly altered in its constitution. This is due not only to the development of special parts, such as the pons, the cerebellum, tectal plate and special nerve tracts that unite the cerebral and spinal centres, but especially to the fact that the structure of the head is older and more complex than that of the body [16]. In the head region another element appears, a *ventral* mesodermal somite or branchiomere, in addition to the *dorsal* mesodermal somite seen in the trunk region (Fig. 116). In the branchiomeres arise the gill arches, which are so apparent in the human embryo at the end of the 1st month. In the mid- and hind-brain special centres and nerves are developed in

fore-brain. The cerebral cortical paths develop in the marginal zone of the basal plates and form the *crura cerebri*, while the afferent paths—the median lemniscus—develop in the mantle zone, the *tegmentum*. In this zone, too, appears the red nucleus, but as yet its neuroblasts have not been traced to their source.

Three Neural Flexures (see Figs. 101, 105, 107).—The *pontine flexure*, a convexity forwards of the pons, has already been mentioned; it is the result of the elongation of the neural plates of the hind-brain due to the proliferation of the neuroblasts and the production of the cerebellar plates. The *nuchal flexure* is concave forwards, and occurs between the medulla and cord in the 4th week, becoming undone as the neck develops at the end of the 2nd month. This flexure is compensatory and of but small import; on the other hand, the cephalic or *anterior flexure*, whereby late in the 3rd week of foetal life the fore-brain appears as a downward and forward development until it comes to lie on the ventral aspect of the cephalic end of the notochord, leads to a great alteration in the form and relationships of the fore- and mid-brains, and is of great importance (Fig. 107). Even in embryos of the lowest vertebrate types the expansion and bending of the anterior end of the neural tube is apparent. The mid-brain by this flexure comes to be, for a short time, the most anterior part of the neural canal; the fore-brain is doubled under the notochord. Round the projecting end of the notochord—projecting between the mid- and fore-brains—are developed the posterior clinoid processes and *dorsum sellae*. The *dorsum sellae* marks the position of the anterior flexure in the adult brain. The *tentorium cerebelli* is developed between the mid-brain and fore-brain, and lies at first at right angles to the axis of the mid-brain, but the subsequent great growth of the cerebrum forces it backwards and downwards until it becomes a horizontal partition between the cerebellar and cerebral chambers of the skull.

Subcommissural Organ.—For some time it has been known that the *ependyma* on the roof of the mid-brain of lower vertebrates, immediately behind the posterior commissure (see Fig. 115), is modified to form a peculiar area of high columnar cells. The cells are related to a certain very large fibre (Reissner's fibre), which descends ventral to the central canal of the spinal cord in fishes and amphibians. Dendy and Nicholls [14] have shown that this *ependymal structure*, to which they have given the name of *subcommissural organ*, occurs in all vertebrates, including man. It is quite apparent in the human foetal brain, but is soon reduced to a vestige. The fibres are not nervous in nature. The function and significance of the structure are unknown. It is not only by the temporary appearance of this organ that the human mid-brain

the cranial part of the neural crest is represented as sending ganglion cells to two regions of the head—to the site of the lateral line organ of lower vertebrates and to the epibranchial placodes. Representatives of these structures do appear in the human embryo in the 4th week, but

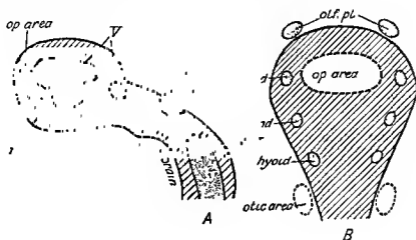


FIG. 117.

they appear to contribute neuroblasts to the head nerves—not to receive them [18].

Segmental Arrangement of Cranial Nerves.—We have seen that seven neuromeres can be recognized in the hind-brain during the 4th week of development, and we may assign two segments or neuromeres to the mid-brain. But when we look at the ganglia and nerves of an embryo in the 6th week of development (Fig. 118) it will be realized that it is impossible to assign a cranial or head segment to each of these. We have seen (p. 111) that the segmentation of the spinal cord is secondary to that of the somatic mesoderm. The same is true of the mid- and hind-brains; their real segmentation is that determined by the mesodermal segmentation of the head region. In the human embryo it is easy to see that the VIIth nerve enters the second or hyoid arch and may be regarded as the nerve of the hyoid segment—which is to be reckoned as the 3rd segment of the head—but the nerve of the segment arises from the 4th neuromere of the hind-brain; while the nucleus of the VIth apparently arises from the 5th. We shall regard both of these neuromeres as belonging to the 3rd cranial segment. In this segment of the head, then, we have an approach to the full complement of nerve elements found in a typical

connection with the gill arches. In the spinal cord there were two columns of motor nerves in the basal lamina, one for the somatic or voluntary muscles of the body, another for the visceral musculature, the splanchnic, but here a third or intermediate column is added—the motor cells for the muscles connected with the gills (Fig. 103). The branchial—or lateral somatic—nerves are represented in the mid- and hind-brain by the motor or ventral root of the Vth nerve, by the motor part of the VIIth, by the parts of the IXth, Xth, XIth which supply striated muscles. The presence of branchial arches in the head region gives rise to a more complex arrangement of the nerve ganglia (Fig. 117). In the trunk region the neural crest gave origin to posterior root ganglia, the ganglia of the sympathetic chain (prevertebral), and other ganglia

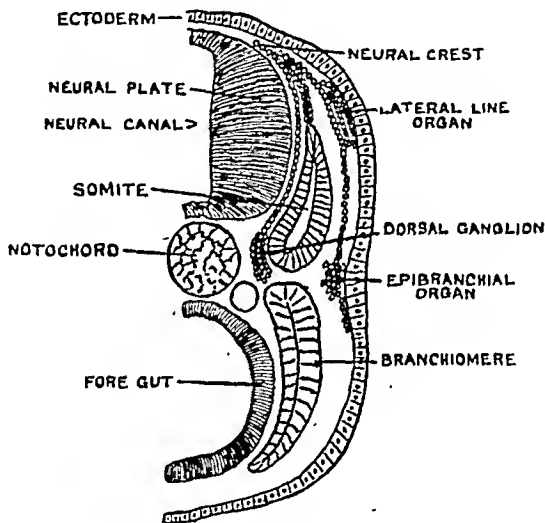


FIG. 116. Diagrammatic section across the posterior region of the Head of *Ammocoetes*—the immature form of the lamprey—to show a branchiomere and the ganglia derived from the neural crest of the hind-brain. (After Froiep.)

stationed in front of the spine. The same ganglionic masses are developed in the hind- and mid-brains, but their arrangement is peculiar.

In the head region the neural crest differs from that of the trunk region in three respects. (i) In the head region the "crest" is divided into anterior, middle and posterior parts [17]. The anterior part, arising from fore, mid and anterior part of the hind-brain, gives origin to all ganglionic cells connected with the Vth nerve (Fig. 117, A). The middle part of the crest, arising from the 4th (middle) neuromere of the hind-brain, gives origin to the ganglia of the VIIth and VIIIth nerves; while the hinder part of the "crest" gives origin to the ganglia of the IXth and Xth nerves. (ii) The "crest" is not separated from the edge of the medullary plate, as in the spinal cord, but comes away from the deep aspect of the plate in the form of a delamination. (iii) In Fig. 116

mastication (lateral somatic or branchial root), the somatic sensory by the maxillary and mandibular divisions of the Vth nerve. The sensory root of the Vth nerve has spread its dominion until it now forms connections with all the segments of the mid- and hind-brain, and even reaches the upper segments of the spinal cord. There are no sensory somatic fibres in the nerves of the 4th, 5th, 6th and 7th cranial or branchial segments with the exception of the auricular branch of the vagus. The IXth, or glosso-pharyngeal, is the nerve of the 4th cranial segment and contains lateral somatic, efferent and afferent splanchnic fibres (to otic ganglion). The vagus and bulbar roots of the spinal accessory represent the splanchnic efferent and afferent nerves of the 5th, 6th and 7th segments—the most important segments in the neural tube, for they contain the nerve centres which dominate the heart, the lungs and the greater part of the alimentary canal. The vagus and spinal accessory contain lateral somatic fibres of the 5th, 6th and 7th cranial segments [20]. The somatic motor roots of the 5th, 6th and 7th cranial segments are represented by the fasciculi of origin of the XIIth nerve—the motor nerve of the tongue. The ganglia of the VIIIth (geniculate), of the IXth (upper or jugular and lower or petrosal) and of the Xth (upper or jugular and lower or nodosum) contains two kinds of nerve-cells: splanchnic motor and splanchnic sensory. Thus in the cranial region, cells which in the spinal region are placed in separate ganglia, posterior root and prevertebral, occupy the same ganglionic mass. It will be thus seen that embryology and comparative anatomy supply a clue to the manner in which the cranial nerves are arranged. The basis of that arrangement is strictly a physiological one, but the specialization in certain segments which has occurred in the course of evolution has destroyed the original simplicity of their arrangement. Further mention of the cranial nerves will be made in dealing with the nose, eye, ear, face and visceral arches.

In the human embryo vestiges of posterior roots and ganglia may appear on the hinder hypoglossal fasciculi (Frobie's ganglion); we may infer that at one time the occipital segments had nerves with anterior and posterior somatic roots [21]. Streeter also observed that the spinal rootlets of the XIth nerve have vestigial ganglia (visceral sensory) on them when first formed (Fig. 118).

NOTES AND REFERENCES

[1] I use the term "inferior medullary velum" as equivalent to the whole of the roof plate of the IVth ventricle. Other authors have restricted it to the part which retains a medullary structure, namely, the part attached to the floccular lobe. Except for this part the roof plate is made up of ependyma and pia mater, sometimes distinguished as the *tela choroidea*. See Hochstetter, F., *Zeitsch.*

cranial segment. The somatic motor fibres are represented by the VIth nerve (to the external rectus); the lateral somatic motor or branchial by the motor fibres of the VIIth or facial; the splanchnic efferent or motor by the secretory fibres of the chorda-tympani of the VIIth; the afferent or splanchnic sensory by the gustatory fibres of the VIIth (chorda tympani and great superficial petrosal); the somatic sensory fibres by the VIIIth or auditory nerve. The cochlear and vestibular ganglia represent a modified posterior root ganglion; the submaxillary ganglion—a vagrant sympathetic ganglion. Thus the 4th neural segment has become associated with the hyoid (2nd visceral) arch, the eye and the ear.

In the other segments of the head there have been great changes and

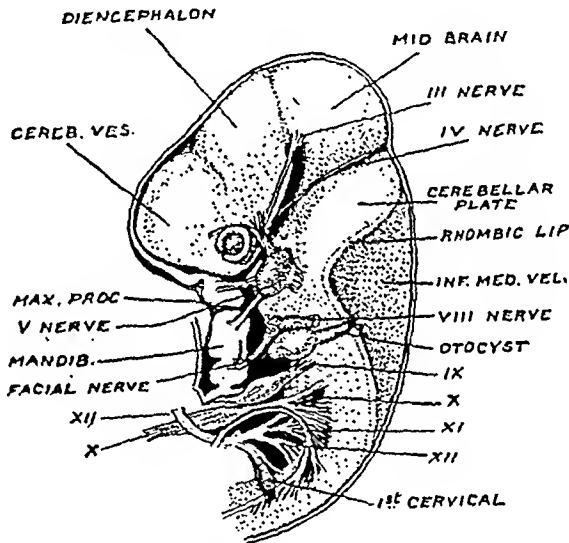


FIG. 118. The Nerves and Ganglia of the Mid- and Hind-Brain of an Embryo at the end of the 6th week of development. (After Streeter.)

reductions. The first or premandibular segment has a composite nerve, the IIIrd or oculo-motor. It contains somatic motor fibres (to the muscles of the eye-ball); sensory or proprioceptive fibres; splanchnic motor fibres (from Westphal-Edinger nucleus to ciliary muscle and sphincter of iris); the long root to the ciliary ganglion contains sensory somatic fibres (Kiss). The ciliary ganglion represents a vagrant sympathetic ganglion of the first segment. To this segment must also be assigned the ophthalmic division of the Vth. Although this nerve represents the posterior root of a spinal nerve, yet its nucleus or ganglion is situated within the mid-brain [19].

The nerves of the 2nd or mandibular segment are represented by the IVth or trochlear nerve (somatic motor), the nerves to the muscles of

mastication (lateral somatic or branchial root), the somatic sensory by the maxillary and mandibular divisions of the Vth nerve. The sensory root of the Vth nerve has spread its dominion until it now forms connections with all the segments of the mid- and hind-brain, and even reaches the upper segments of the spinal cord. There are no sensory somatic fibres in the nerves of the 4th, 5th, 6th and 7th cranial or branchial segments with the exception of the auricular branch of the vagus. The IXth, or glosso-pharyngeal, is the nerve of the 4th cranial segment and contains lateral somatic, efferent and afferent splanchnic fibres (to otic ganglion). The vagus and bulbar roots of the spinal accessory represent the splanchnic efferent and afferent nerves of the 5th, 6th and 7th segments—the most important segments in the neural tube, for they contain the nerve centres which dominate the heart, the lungs and the greater part of the alimentary canal. The vagus and spinal accessory contain lateral somatic fibres of the 5th, 6th and 7th cranial segments [20]. The somatic motor roots of the 5th, 6th and 7th cranial segments are represented by the fasciculi of origin of the XIIth nerve—the motor nerve of the tongue. The ganglia of the VIIth (geniculate), of the IXth (upper or jugular and lower or petrosal) and of the Xth (upper or jugular and lower or nodosum) contains two kinds of nerve-cells: splanchnic motor and splanchnic sensory. Thus in the cranial region, cells which in the spinal region are placed in separate ganglia, posterior root and prevertebral, occupy the same ganglionic mass. It will be thus seen that embryology and comparative anatomy supply a clue to the manner in which the cranial nerves are arranged. The basis of that arrangement is strictly a physiological one, but the specialization in certain segments which has occurred in the course of evolution has destroyed the original simplicity of their arrangement. Further mention of the cranial nerves will be made in dealing with the nose, eye, ear, face and visceral arches.

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Anat. Entwickl., 1933, 101, 211; Johnston, T. B., *Jour. Anat.*, 1934, 68, 471; Wilson, J. T., *ibid.*, 1937, 71, 423.

[2] Prof. J. E. Frazer (*Manual of Embryology*, 1940) describes the olivary bodies as arising in the ventro-lateral area of the medullary plate.

[3] See *The Comparative Anatomy of the Nervous System of Vertebrates, including Man*, by C. U. Ariëns Kappers, G. Carl Huber, and Eliz. C. Crosby, 1936; *Three Lectures on Neurobiotaxis*, by C. U. Ariëns Kappers, 1928. Prof. Raymond Dart, under the *Law of Infiltration*, has applied Neurobiotaxis to explain the evolution of the ganglionic masses and cortical areas of the cerebrum and cerebellum (*Acta Zoologica*, 1925, 6, 223; *Jour. Anat.*, 1924, 58, 181). Prof. Wood-Jones has coined the term "cytoclesis" to cover all phenomena of inter-cellular attraction (*Lancet*, 1924, 1, 484; *Matrix of the Mind*, 1928).

[4] Flexner and Stiehler, *Anat. Rec.*, 1938, 70, 27 (suppl.).

[5] Weed, Louis, *Anat. Rec.*, 1916, 10, 256; *Amer. Jour. Anat.*, 1923, 31, 213; *Jour. Anat.*, 1938, 72, 181; Woollard, H. H.; *ibid.*, 1924, 58, 89; Clark, W. E. Le Gros, *ibid.*, 1920, 55, 41; Stopford, Sir J., *ibid.*, 1930, 64, 257; Gladstone and Dunlop, *ibid.*, 1927, 61, 360; Rogers and West, *ibid.*, 1931, 65, 457; Peter, K., *Zeitsch. Anat. Entwickl.*, 1937, 106, 398; Cohen and Davies, *Jour. Anat.*, 1938, 72, 23, 430; Weiss, P., *Anat. Rec.*, 1934, 58, 299.

[6] Wilson, J. T., *Jour. Anat.*, 1906, 40, 210.

[7] See references to Flexner and Stiehler, note [4]; to Cohen and Davies, note [5].

[8] See Ariëns Kappers, note [3]; Streeter, G. L., in Kiebel and Mall's *Manual of Embryology*, 1912; Frazer, J. E., *Manual of Embryology*, 1931; Elliot-Smith, Sir G., *Jour. Anat.*, 1903, 37, 329; Abbie, A. A., *Proc. Roy. Soc.*, 1934, 115 (B), 504; Botterell and Fulton, *Jour. Comp. Neur.*, 1938, 69, 31; Hindenach, J. C. R., *Jour. Anat.*, 1931, 65, 283 (in Sphenodon); Larsell, O., *Jour. Comp. Neur.*, 1936, 63, 65 (in opossum); 1936, 64, 275 (in bat); Ziehen, Th., *Anat. Anz.*, 1935, 80, 25; Dow, R. S., *Jour. Comp. Neur.*, 1938, 88, 297.

[9] See reference to Hindenach, J. C. R., note [8].

[10] For reviews of the evidence bearing on localization of function in the cerebellum, see works mentioned in note [8] by Botterell and Fulton, Ariëns Kappers and Abbie; see also *Text Book of Neuro-Anatomy*, by Prof. Kuntz, 1937, and the late Prof. Woollard's *Recent Advances in Anatomy*, 1927.

[11] I have written as if there is no doubt that all four elements are present in the mid-brain—floor-plate, roof-plate, basal and alar laminae. Dr. K. F. Kingsbury believes that the floor-plate ceases at the isthmus (hinder end) of the mid-brain (*Jour. Comp. Neur.*, 1922, 34, 461). He is also of opinion that the basal lamina is not represented in the front part of the mid-brain. Prof. Frazer holds that the nucleus of the IVth nerve, although developed in the basal lamina, is carried to its peculiar position in the roof-plate during a migration of basilar neuroblasts (*Jour. Anat.*, 1929, 63, 7). See also Addens, J. L., *Zeitsch. Anat. Entwickl.*, 1933, 101, 306.

[12] Goldby, F., *Jour. Anat.*, 1937, 71, 332.

[13] Lucas Keene, M. F., *Jour. Anat.*, 1938, 72, 488; Lucas Keene and Hewer, *ibid.*, 1933, 67, 522; Windle, W. F., *Jour. Comp. Neur.*, 1936, 63, 139.

[14] *Quart. Jour. Mic. Sc.*, 1913, 58, 1.

[15] *Jour. Anat.*, 1938, 72, 488.

[16] See reference to Prof. De Lange's work, note [6], Chapter III; also references contained in note [2], Chapter XII.

[17] Baxter and Boyd, *Jour. Anat.*, 1937, 73, 318.

[18] For accounts of the development of the neural crest, see Bartlemez and Evans, *Contrib. Emb.*, 1926, 17, 1; Adelman, H. B., *Jour. Comp. Neur.*, 1925, 39, 19; West, C., *Contrib. Emb.*, 1930, 21, 25; Atwell, W. J., *ibid.*, 1930, 21, 1; Schneider, A. J., *Anat. Rec.*, 1928, 38, 321; Frazer and Whitehead, *Brain*, 1925, 48, 458 (Gasserian ganglion); for epibranchial placodes (in sparrow), see Goldby, F., *Jour. Anat.*, 1928, 63, 135.

[19] Kiss, F., *Jour. Anat.*, 1932, 66, 488 (finds that cells of ciliary ganglion are similar to those of a posterior root ganglion); see also on this matter article by Blair and Davies, *Lancet*, 1933, 1, 1113. For ganglia of vagus, see Fahmy, N., *Jour. Anat.*, 1927, 61, 298.

[20] The striated muscles supplied by the XIth nerve are assigned to the somatic musculature by Dr. J. L. Addens (*Zeitsch. Anat. Entwickl.*, 1933, 101, 306).

[21] Wilson, J. T., *Jour. Anat.*, 1925, 59, 345; Pearson, A. A., *Jour. Comp. Neur.*, 1938, 68, 263; Tarkhan, A. A., *Zeitsch. Anat. Entwickl.*, 1936, 105, 349; Barnard, J. W., *Jour. Comp. Neur.*, 1936, 65, 503.

CHAPTER X

THE FORE-BRAIN OR PROSENCEPHALON

Origin of the Cerebrum.—It is in connection with the fore-brain that the most distinctive and most complex of all human structures arises—the cerebrum. If we confine our attention purely to the developmental changes which occur in the fore-brain of the human embryo, we shall understand very imperfectly the origin and nature of the human brain. It is true that on developmental evidence alone we may infer that the fore-brain, although situated at the anterior extremity of the neural

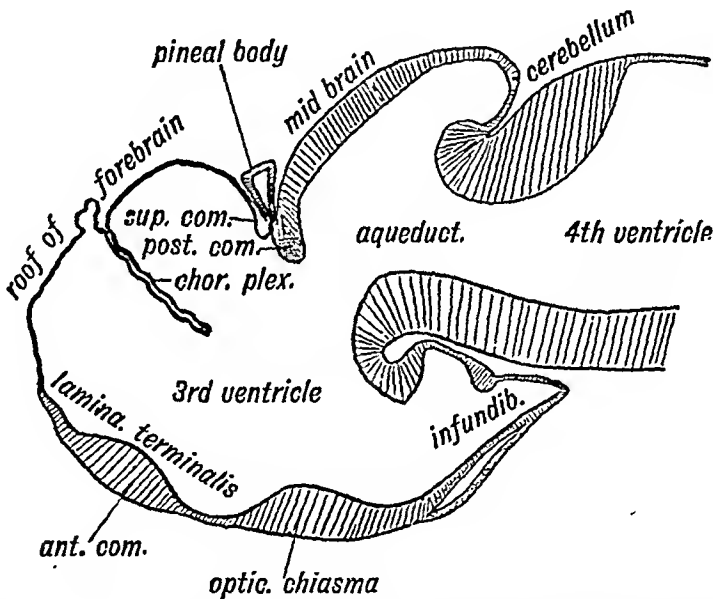


FIG. 119. Longitudinal section of the Brain of a Larval Fish, to show the primary form and relations of the fore-brain. (Kupffer.) Note especially that the whole roof is formed by a choroidal velum.

tube, does not represent a prolongation of all the elements of the tube: the floor plate disappears as the 3rd ventricle is entered, and so does the basal (motor) lamina, but not all of it. We shall see that there is a continuation of a most important representation of the sympathetic element of this lamina in the form of the *hypothalamus* (Fig 122). The element chiefly represented in the fore-brain is the alar or dorsal lamina, which we know to subserve sensory functions. To obtain a proper appreciation of the fore-brain, however, one must study the fore-brain in the lowest of vertebrates—the Lamprey. In Fig. 119 the brain of

this primitive fish is represented. The fore-brain is made up of two parts—a posterior, the *thalamencephalon* or *diencephalon*, with which the retinae and optic tracts are connected, and an anterior or *telencephalon*, in which the olfactory nerves terminate. The two parts of the fore-brain have thus arisen in connection with the sense of sight and the sense of smell; secondary nerve masses have arisen in these two parts of the fore-brain—the optic thalamus in the posterior and the corpus striatum in the anterior; but the optic thalamus receives not only nerve tracts connected with the sense of sight, but other sensory tracts connecting it with all the systems of the body—skin, muscles, joints, ear, etc.—and thus becomes a centre for the orderly distribution of sensory messages to all parts of the fore-brain—particularly to the cerebral

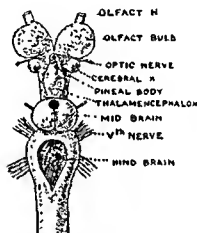


FIG. 120. The Brain of the Lamprey from above. (After R. H. Burne.)

cortex. Its connections with the fore-brain are reciprocal; it receives as well as dispatches. The corpus striatum—the secondary mass in the anterior or olfactory part, the telencephalon—deals with messages received from both thalamus and cortex, serving as a great regulating and controlling centre. In the brain of the lamprey the mid-brain and the two parts of the fore-brain form a “federation of centres” [1]. In mammals the telencephalon becomes the dominant part; the cerebral hemispheres arise in it. Thus our cerebral hemispheres have arisen in connection with parts which have become insignificant—the olfactory nerve centres. The telencephalon has received and formed communications with all parts of the central nervous system, and become the central exchange of all sensory impulses and also the seat of consciousness and of will.

The Fore-Brain of the Human Embryo.—In the 4th week of development there is a resemblance between the human fore-brain and that of

a fish : both are of a simple vesicular form (compare Figs. 119 and 121). In some respects the fish's brain is the more instructive, because its parts are clearly differentiated. In the fish the roof of the 3rd ventricle—the name given to the central canal of the thalamencephalon—contains no nerve tissue ; it is membranous, and forms a choroid plexus. The pineal body arises from the posterior part of the roof, immediately in front of the posterior commissure (Fig. 119). The representatives of those parts are seen in the roof of the 3rd ventricle of the human embryo (see Figs. 121, 122, 123). On the narrow floor of the 3rd ventricle are to be seen all parts of the hypothalamus, including the infundibular part of the pituitary body and the optic chiasma—or the plate in which the chiasma will be formed. In both the fish and the human embryo the

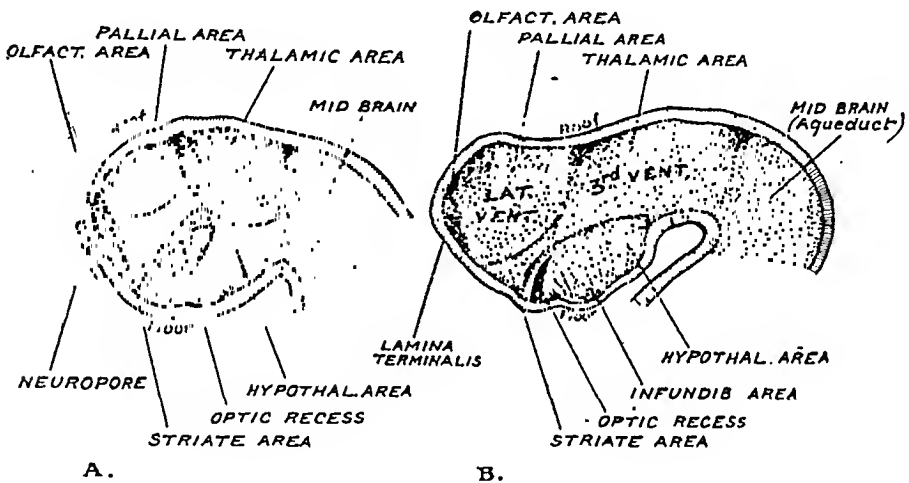


FIG. 121. Sections of the Fore-Brain at the beginning (A) and near the end (B) of the 4th week of development.

anterior wall of the 3rd ventricle is formed by a plate of neural tissue—the *lamina terminalis*.

Parts developed in the Wall of the Fore-Brain.—When a model of the fore-brain of an embryo in the 4th week of development is laid open, as in Fig. 121, it is possible to identify its two main divisions—a posterior or *thalamencephalon*, its central cavity becoming the 3rd ventricle (Fig. 121, B), and an anterior or *telencephalon*, which will enclose the lateral ventricle. At the junction of these divisions, but yet lying distinctly in the wall of the thalamencephalon, is seen the wide evagination (Fig. 121, A) which gives rise to the *optic vesicle*—the basis in which the retina and optic nerves will develop. A section across the thalamic region of the fore-brain at this stage shows a right and left lateral plate, their basal margins being united by a trough-like floor provided by the hypothalamus, while their dorsal margins are joined by a roof plate—

which, late in the 2nd month, becomes converted into the choroid plexus of the 3rd ventricle, just as was the case with the roof plate of the 4th ventricle. The lateral plates show the usual three zones during the 4th week—an inner endymal, in which an active cellular proliferation is giving rise to the thalamus and other nuclear masses; a middle or mantle zone, into which the proliferating neuroblasts spread; and an outer or marginal, which in the 3rd month becomes invaded by the great trackways leading to and from the fore-brain. At this early stage, too, a groove can be seen running obliquely on the lateral wall of the 3rd ventricle, from the floor of the mid-brain to the optic recess (Fig. 122), indicating a division of the lateral plate into an upper or thalamic and a lower or hypothalamic region. In the upper region will be differentiated the *optic thalamus* [2], with, over it and just under the roof-plate (Fig. 122), the *epithalamus* (pineal body, ganglia of the habenula, striac

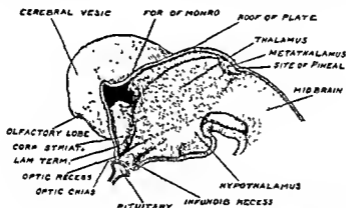


FIG. 122. The Thalamencephalon towards the end of the 6th week of development

pineales or medullares), while in the lower region and in the floor plate are differentiated the *hypothalamus*, including the infundibular stalk of the pituitary body, the tuber cinereum, the mamillary bodies and the posterior perforated space. Here we are chiefly concerned with the walls of the 3rd ventricle, but it may be noted in Figs. 121, *A* and *B*, that the three areas of the telencephalon can also be identified: the cortical or pallial area of the cerebral evagination, the striate area—forming a junctional zone between the thalamic and hypothalamic regions of the 3rd ventricle and the pallial area of the lateral ventricle (Fig. 121, *B*)—and an olfactory area. At the beginning of the 4th week (Fig. 121, *A*) the *neuropore* is still open, and the olfactory areas which will appear at each side of the closed opening can hardly be said at this time to be differentiated.

By the end of the 6th week certain notable changes have occurred in the fore-brain (Fig. 122); the cerebral vesicle is now rapidly expanding,

its hinder or occipital end beginning to grow over and cover the roof and lateral walls of the thalamencephalon. The opening of the lateral ventricle has become relatively smaller, owing to the upgrowth and more intimate fusion of the *corpus striatum* with the optic thalamus. In the hypothalamic region we can now see a recess behind the optic chiasma, indicating the downgrowth of the infundibular process of the pituitary body (hypophysis), and in contact with the floor plate an area of ectoderm developed from the embryonic mouth or stomodaeum, which will form the anterior or glandular part of the pituitary. The roof plate is now beginning to be converted into a secretory structure—the choroid plexus of the 3rd ventricle. The roof plate can be seen to extend (Fig. 122) from a slight dip or fold over the foramen of Monro to the region of the posterior commissure at the anterior border of the mid-brain.

In Fig. 123, which represents in a diagrammatic manner the simple

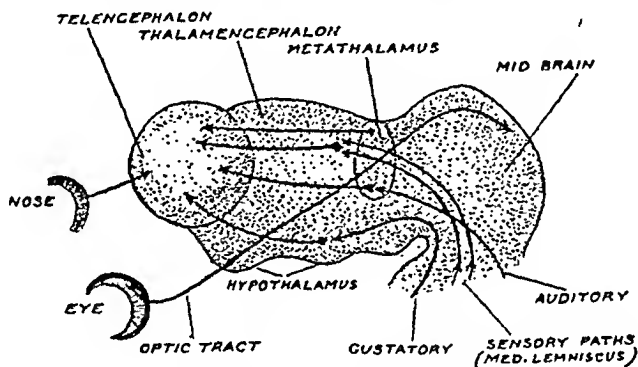


FIG. 123. Diagram of the Embryonic Fore-Brain, to show how its various parts become linked to sensory tracts. (Elliot-Smith.)

fore-brain of an embryo at the end of the 1st month of development, there have been represented—following a scheme devised by the late Sir G. Elliot-Smith—the great sensory pathways which terminate in the thalamencephalon and make it into the great court of sensory appeal. These fibre tracts, which do not begin to make their way through the mid-brain from the medulla and cord until the end of the 3rd month of development, are depicted by simple arrows—the medial lemniscus and auditory tract ending in the optic thalamus, while the gustatory tract ends in the hypothalamic region. Relays of fibres commencing in the thalamencephalon carry optic, auditory, gustatory and common sensory impulses to the telencephalon—the highest court of sensory appeal. It is when this broad conception of the relationship of the fore-brain to the sensory tracts is grasped that we begin to understand the reason for the transformation of the simple fore-brain of the embryo into the elaborate cerebrum of the adult. The thalamus and fore-brain reach their highest point of evolution in man.

In the fully developed human brain the thalamus dominates the lateral wall of the 3rd ventricle, but even as late as the 3rd month of foetal development (Fig. 124) it remains relatively small, while the epithalamus and hypothalamus are relatively large. In the adult brain the opposite is the case, and this is due not to any reduction in the development or function of the hypothalamus or epithalamus, but to the extreme growth of the human thalamus. All three parts—epithalamus, thalamus and hypothalamus—are interposed between the olfactory area of the telencephalon in front and the centres of the mid-brain behind (Fig. 124). All

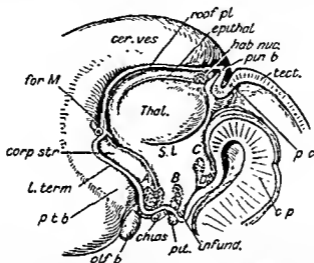


FIG. 124. Sagittal section of the Human Brain in the 3rd month of development, exposing the lateral wall of the 3rd ventricle to show the small size of the thalamus (Thal.) at this date. (After Le Gros Clark.)

A, B, C, D, sites at which the anterior, the middle, and the two posterior groups of hypothalamic nuclei are developed.

Olf. b., olfactory bulb; chias, chiasma; pit., anterior pituitary; infund., infundibulum.

three are traversed by nerve tracts which serve to link them up with small brain and with mid-brain.

The *Lamina terminalis* forms the anterior or terminal wall of the simple fore-brain of the 4th-week embryo (Fig. 121, B); it is completed by the closure of the neuropore (Fig. 121, A). When the cerebral vesicles grow out it becomes demarcated as a plate stretching from the foramen of Monro above to the optic chiasma below (Fig. 122), and joining together the olfactory areas of the cerebral vesicles. This simple plate, which comes to form the anterior wall of the 3rd ventricle, begins to assume great importance in the 2nd month, because it serves as a bridge for the crossing of nerve tracts between the right and left halves of the telencephalon. The development of these commissural tracts will be mentioned later; in the meantime it may be pointed out that

part of it retains almost its embryonic state in the adult and forms the lamina cinerea which closes the anterior wall of the 3rd ventricle between the optic chiasma below and the corpus callosum above.

Hypothalamus [3].—I have said that the hypothalamus—the complex of structures which forms the floor of the 3rd ventricle—represents a continuation of the visceral or sympathetic element of the basal lamina. This statement is founded on the remarkable discoveries now being made as regards the functional nature of the hypothalamus. These discoveries show it to be the headquarters of the sympathetic or visceral system of the body. Comparative anatomy, too, shows the hypothalamus to be amongst the most ancient parts of the human brain—perhaps the most ancient. In its walls, during the 2nd month, there is differentiated a scattered series of nerve cells in three rather ill-defined groups—*anterior, middle and posterior* (Fig. 124). The earliest nerve tracts to appear in the brain arise in connection with these centres. Through these tracts the hypothalamus becomes linked during the 2nd month of development with olfactory centres, which lie immediately in front of it, and with centres in the mid-brain just behind it, both tectal and tegmental. In the course of development tracts are established to carry to it stimuli from olfactory, gustatory and visceral centres. Also efferent paths are established which give the hypothalamus dominion over the visceromotor centres of brain-stem and cord. The posterior centres are connected with the sympathetic stations of the medulla and spinal cord by relays of fibres; it dominates the lower centres in the structures just named. The posterior centres receive communications from the anterior (supraoptic) and middle (tuberal) centres. All are concerned in the conduct and management of the animal or vegetative functions of the body—digestion, assimilation, metabolism, heat regulation, sexual life, sleep, temper, etc. Later communications are developed between hypothalamus and thalamus (in which I include the subthalamus or ventral thalamus). Then, through the thalamic centres, two parts of the human cerebrum become connected with the hypothalamus. These are the cingular gyrus (gyrus fornicatus), which is sensory or receptive in function, and the anterior frontal cortex, which can thus exert an inhibitory or controlling influence on the hypothalamic centres. The establishment of such connections made human civilization possible [5].

In Fig. 125 the nerve supply to the pituitary body is indicated by the lowest arrow. The fibres of supply arise from cells situated in the anterior or supra-optic group and end chiefly in the neural lobe, but fibres have been traced to the intermediate and anterior glandular parts. As evidence now stands it seems best to regard the pituitary as the hand-maid of the hypothalamus. We have seen that the hormones which

regulate the ripening of the gonads are formed in the pituitary [4]. There are grounds for believing that the functions of the pituitary are

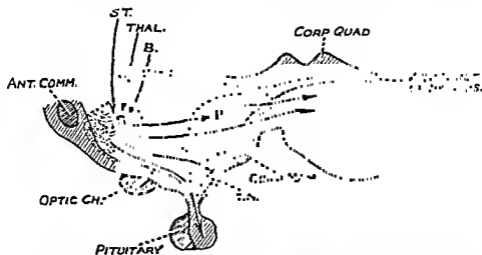


FIG. 125 Diagram to show the position of the three chief Nerve Centres in the floor of the 3rd ventricle (hypothalamus). The arrows indicate the chief connections of these centres. (Prof. John Beattie.)

S, Supra-optic group of nuclei; *P*, posterior group of nuclei; *T.N.*, tuber nucleus; *ST*, fibres from stria terminalis; *Thal.*, fibres from thalamus, *B.*, fibres from medial fore-brain bundle. The other arrows indicate connecting and efferent tracts

timed by centres situated in the hypothalamus. Similarly with the growth-regulating hormones formed within the pituitary.

Glands arising from the Walls of the 3rd Ventricle.—We have seen that the roof plate of the 3rd ventricle is converted into a secretory structure—the choroid velum. We now proceed to note the manner in which two

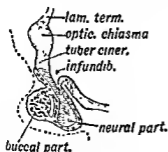


FIG. 126

FIG. 126 Section of the Pituitary Body of a Human Foetus in the 5th month. (Edinger.)



FIG. 127.

FIG. 127. Showing the position of the Pineal Body and its commissure and ganglion.

remarkable glandular bodies arise in connection with the 3rd ventricle—the pituitary in relationship to the anterior part of its floor and the pineal from the hindmost part of its roof. We must suppose that their functions are closely related to those of the central nervous system. The position and connections of these two bodies will be seen in Figs. 126, 127. A sagittal section of the pituitary body of a foetus of the 5th

month is drawn in Fig. 126, showing the neural part, derived from the floor of the 3rd ventricle, and the buccal, derived from the ectoderm of the primitive mouth. The glandular mass of the buccal element is divided by its central cavity into a larger anterior part or lobe and a smaller, paraneural or intermediate part, applied to the neural element. Besides these *two* parts there is a third, the lateral or tuberal part, which is seen on section in Fig. 126, applied as a plate to the neck of the infundibulum. The pineal body of a newly born child is represented in Fig. 127; it is about the size of a wheat grain, resting on the roof of the mid-brain between the superior corpora quadrigemina. On each side are seen the upper surfaces of the optic thalami. Running forward from it are the *striae pineales*; at each side is the habenula with its nuclei.

Pituitary Body [6].—As is so often the case in the development of the

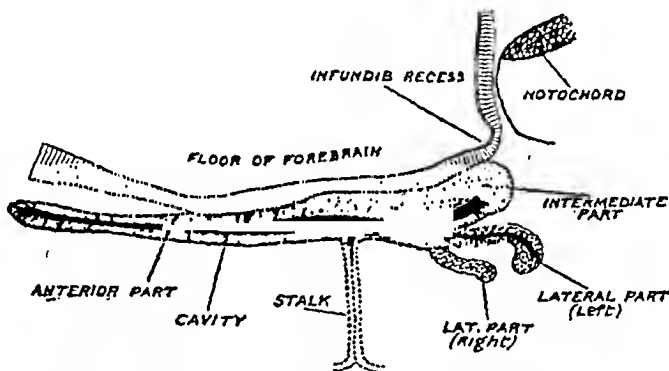


FIG. 128. Sagittal section of the Pituitary Body of a Pup Dog-Fish.
(After Baumgartner.)

human body, procedures which take place obscurely in man present themselves with almost diagrammatic sharpness in low vertebrates—particularly in selachians, of which the dog-fish may be taken as a type. The original saccular form of the pituitary body and its division into three parts or lobes are well seen in the pup dog-fish (Fig. 128). The original stalk is indicated, and the three parts into which the sac becomes divided by the growth and proliferation of the epithelial cells in its walls are shown. The lateral or tuberal parts arise as right and left diverticula near the root of the stalk. The tuberal part, as a distinct element of the pituitary complex, was first recognized by Dr. Tilney in 1913 [7], but since then its presence has been noted in all vertebrates, including man. The lateral or tuberal parts as they expand become applied to the infundibular region of the floor of the 3rd ventricle, their cells invading the arachnoid and occupying its meshes.

By the end of the 4th week the basis of the buccal part of the pituitary

can be recognized in the roof of the primitive mouth or stomodaeum (Fig. 129, *A*), just in front of the *oral plate*, which at this time closes the anterior end of the fore-gut. At an earlier stage, when the neuropore is still open (Fig. 121, *A*), the roof plate of the stomodaeum runs into the floor plate of the fore-brain at the neuropore, the two being in the closest contact. Thus the neural and glandular (ectodermal) constituents are in contact from the beginning; if they are not in contact, development of the gland fails [8]. The stomodaeum is lined with ectoderm, and it is therefore an ectodermal enclosure, known as *Rathke's pocket*, which goes to form the buccal part of the pituitary. It will be noted that the ectodermal element is closely applied to the floor of the fore-brain from the start; in the 5th week the adjacent part of the neural floor begins

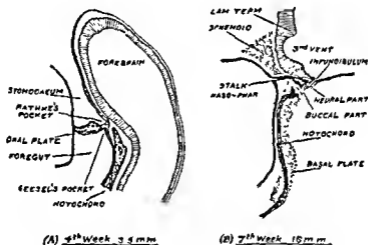


FIG. 129. Development of the Pituitary. *A*, its condition in a human embryo 4 weeks old; *B*, in an embryo in the 7th week of development. (Rudel.)

to grow out, and becomes the infundibular process. One other point should be noted: just behind the upper attachment of the oral plate the endoderm of the fore-gut forms a slight pocket. Seessel found that in some animals (birds) this pocket also took part in the formation of the pituitary, and hence it is called *Seessel's pocket*. This element, however, does not share in the final production of the human pituitary.

By the 7th week marked changes have occurred (Fig. 129, *B*). The infundibular process (the neural part) is now quite evident; its cavity is still open, becoming filled up in the 9th week. The buccal evagination has assumed a pocket form—pressing against the neural process, its neck having become drawn out into a long stalk, because the base of the skull is then being laid down between the roof of the pharynx and the floor of the fore-brain. The nasal and buccal cavities are being developed, the buccal end of the stalk coming ultimately to lie at the

posterior border of the nasal septum. Usually some fragments of the pituitary stalk persist in the mucous membrane on the roof of the nasopharynx; cases occur in which, owing to a malformation of the base of the skull, the whole pituitary body lies in the posterior part of the nasal septum. By the 9th week the stalk has disappeared, but occasionally a canal in the body of the sphenoid bone of the adult—the *cranio-pharyngeal canal*—marks the site of the embryonic stalk [9].

During the 3rd month the epithelial lining of the pituitary sac grows rapidly, particularly in the anterior part, where glandular masses encroach upon the lumen (Fig. 130), ultimately obliterating all but the central space between the anterior and intermediate parts. The gland encapsules itself in the tissues of the dura mater, branches of the internal carotids and mesodermal tissue entering the glandular masses as they begin to proliferate into the central cavity.

Many theories have been formed to account for the position and forma-

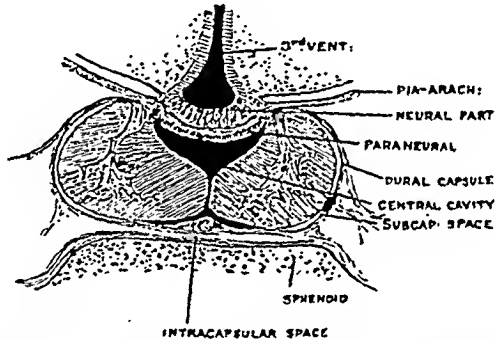


FIG. 130. Coronal section of the Pituitary Body of a Human Foetus at the beginning of the 4th month of development. The section is across the anterior lobe.

tion of the pituitary in the floor of the 3rd ventricle. Its early history has to be sought for amongst our invertebrate ancestors. Gaskell, who regarded the neural or cerebro-spinal canal as the homologue of the invertebrate alimentary canal, homologized the pituitary evagination of the buccal ectoderm with the invertebrate mouth and gullet, and the pituitary body itself with the coxal glands of crustaceans [10]. The pituitary body exercises a curious influence on the growth of the body, especially on certain parts, such as the face and limbs. Disease of the pituitary body may lead to overgrowth of the limbs, as in giants, or of the face, as is seen in cases of acromegaly [11]. It forms certain substances (hormones) which regulate the activities of the ovary, testis and uterus.

As is shown in Fig. 130, the body of the gland is embedded in the dura mater, only its neck lies within the arachnoid [12]. The veins of the infundibular portion form a fine plexus which empties its blood into the sinusoids of the anterior lobe [13]. Certain neural cells in the hypo-

thalamus and in the neural lobe of the pituitary are secretory in nature [14].

Pineal Body or Epiphysis [15].—In recent years it has been shown that both pituitary and pineal bodies secrete substances which have a powerful influence on the development and growth of tissues, that of the pineal being more especially on those parts which undergo changes at sexual maturity. The situation of the pineal body at the hinder end of the roof of the 3rd ventricle is shown in Fig. 127, but its connections—especially with the posterior commissure, habenular commissure and choroid plexus—are better seen in Fig. 115, p. 149. Originally the *Pineal organ* was a complex structure, consisting, as is shown in Fig. 131, of a parietal organ or eye, the organ being socketed in the sagittal suture,

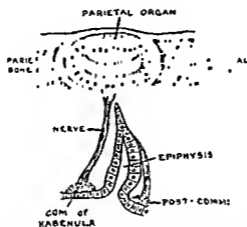


FIG 131. The Pineal Gland (Epiphysis) and Sense Organ in a Lizard. (Oaupe)

and an adjacent glandular structure opening on the roof of the 3rd ventricle [16]. In mammals, as in man, only the 2nd or glandular part, nerve nuclei and commissures are developed. In fossil reptiles and in some forms still living a median eye is formed which perforates, and appears on, the dorsum of the head, between the parietal bones, a relationship which is simulated in the head of the human foetus during the 2nd month (Fig. 114, p. 146). The pineal eye differs from the lateral eyes which grow from the 3rd ventricle as the optic vesicles in that it produces the lens as well as the retina and optic stalk. The retina is inverted—i.e., the apices of the rods and cones point towards the vitreous chamber. The ganglion of the habenula, situated on the dorsal and inner aspect of the optic thalamus (Fig. 127), appears to represent its terminal ganglion, but it must also be remembered that this ganglion receives the pineal stria which arise from various olfactory centres and has communications with hypothalamus, thalamus and mid-brain. The

two ganglia become connected across the roof plate by a commissure (the superior or habenular commissure) (Fig. 127).

The manner in which the pineal body arises in man is shown in Fig. 132. At the posterior end of the fore-brain, and immediately in front of the site of the posterior commissure, the ependymal lining grows out in the shape of a pocket in the 6th week of development. The evaginated cells form a zone of cellular proliferation (Fig. 132, *A*), as we have seen is the case everywhere in the neural tube, but in this instance the cells produced are mainly glandular in nature, there being, however, as Dr. Krabbe

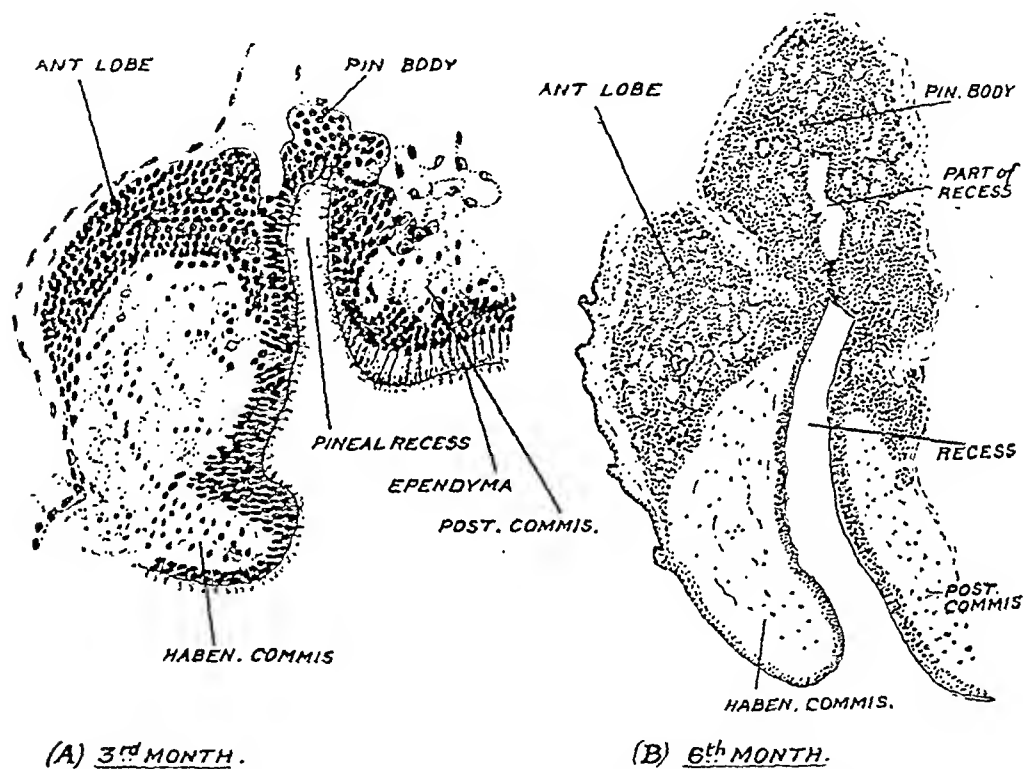


FIG. 132. Showing stages of development of the Pineal Body in the roof of the fore-brain: *A*, in the 3rd month; *B*, in the 6th month. (After Krabbe.)

observed, also some neuroglial and neuroblastic elements. From the anterior wall of the pocket a mass of cells separates early to form an anterior lobe (Fig. 132), while others from the fundus produce a posterior lobe. In the 5th month (Fig. 132, *B*), the pineal body assumes its final form; part of the recess or pocket becomes closed off in the distal part of the gland. The glandular mass is invaded by vascular and mesenchymal tissue, and the same formation of interlacing columns is produced as is seen in the buccal part of the pituitary and in the cortex of the adrenal. In adults only a few of the glandular cords of the pineal persist; often they disappear altogether.

Gladstone and Wakeley [17], who have confirmed and extended Krabbe's observations, find that while the distal part of the cavity of the pineal diverticulum is obliterated by glandular development, the stalk or more proximal part of the recess ultimately merges in the cavity of the 3rd ventricle.

Prof. Le Gros Clark observed [18] that certain nerve fibres which issue from the pineal by its stalk end in the coats of the great vein of Galen and in the proximal part of the straight sinus, within the lumen of which a pacchionian-like granulation projects. There may be here, as he has suggested, a receptor mechanism which regulates the outflow of venous blood from the vessels of the ventricles and thus helps in the control of the pressure of cerebrospinal fluid within them. Cysts or tumours of the pineal frequently compress the veins as they issue from the medullary velum, and so give rise to distension of the ventricles [19].

How it has come about that certain tumours of the pineal body, like those of the cortex of the adrenals, have the power to secrete hormones which bring about an abnormal or premature development of secondary sexual characters still remains an enigma. It is possible that the pineal eye in early reptilian forms may have conveyed stimuli which regulated the maturation of gonads.

We have finished our survey of the structures which arise in the walls of that part of the fore-brain which encloses the 3rd ventricle; we shall proceed in the next chapter to trace the origin of the important structures developed in the walls of that part of the fore-brain (telencephalon) which ultimately encloses the lateral ventricles. Before doing so it may be helpful to turn back and fill in certain details relating to parts we have already surveyed and to touch on matters which will come up for our consideration in the chapter which follows. This can be done best by help of an illustration (Fig. 133), taken from a recent paper by Prof. Judson Herrick [20]. The illustration represents a median sagittal section of the brain of a larval axolotl just entering the swimming phase of its existence. In form, this tubular brain has a close resemblance to that of a human embryo in the 6th week of development (Fig. 122, p. 159). The wall of the axolotl brain has been mapped into structural areas by Prof. Herrick; these areas are also functional in character. There is every reason to believe that if the developing human brain were to be suitably examined the same areas would be found and that they would occupy corresponding positions.

Let us consider first the areas of the cerebral vesicle (telencephalon). Area 1 becomes the olfactory bulb; the ectoderm covering this area becomes transformed into the olfactory placode. The areas 2, 3 are also devoted to the sense of smell, 2 becoming the basis of the pyriform

lobe and 3 that of the hippocampal complex of the human brain. Between the areas 2 and 3 are evolved all the new cortical areas (neocortex) of the mammalian brain. The neocortex makes up the greater part of the human cerebrum. Area 4 (paraterminal) and area 5 (preoptic) are also olfactory in nature and function. Thus it will be realized that the cerebral vesicle arose as an adjunct to the sense of smell.

It is important to note the position of area 6, the strio-amygdalate. It lies at the junction of the first and second divisions of the fore-brain, where the foramen of Monro will be established. Areas 2 and 3 become cortex, but area 6 remains buried; its developing neuroblasts are crowded in the deep or ependymal border, and form deep nuclear masses—the

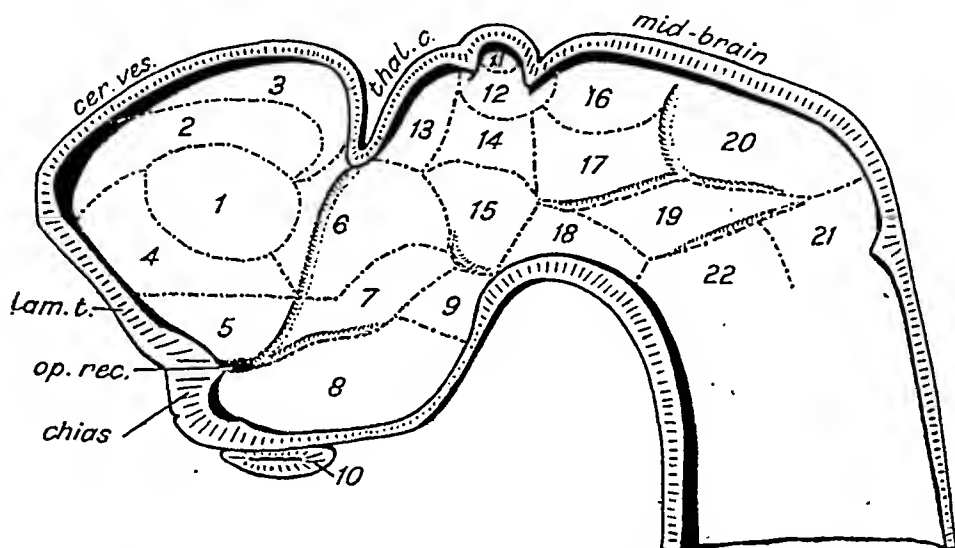


FIG. 133. Median sagittal section of the Brain of a Larval Axolotl mapped into morphological areas. (Judson Herrick.) The areas of the telencephalon (*cer. ves.*) are numbered 1-6; *op. rec.*, optic recess; *lam. t.*, lamina terminalis; *chias.*, section of optic chiasma; the areas of the thalamencephalon (*thal. c.*) are numbered 7-15; those of the mesencephalon (*mid-brain*) are numbered 16-22. For further explanation, see text.

old striate (paleo-striate) and the *old amygdaloid* bodies. Seeing that the more superficial parts of the first or cerebral vesicle are subservient to the sense of smell, we are not surprised to find that the adjacent deep masses of area 6 are of the same nature. They serve as relay stations between the cerebral vesicle and adjoining areas of the thalamencephalon.

Above area 6, between it and the olfactory areas, 2, 3 (Fig. 133), there arose during the evolution of early mammals a new deep nuclear mass, the *new striate* or neostriatum, which is added to the old striate and old amygdaloid to form the *corpus striatum* of higher brains. Thus in that very complex nuclear mass the corpus striatum, at the base of the human brain, we find two elements: the old—the part already evolved in fish and in amphibia; and the new—the part which reaches the climax of its development in the human brain.

We may pass lightly over the areas mapped in the second vesicle, the thalamencephalon or diencephalon. Its cavity becomes the 3rd ventricle. Areas 7, 8, 9 are parts of the hypothalamus, 10 being the hypophysis, or pituitary body, attached to its floor. The epithalamus is represented by areas 11, 12, 13—relatively large areas. The thalamus proper is represented by the rather restricted areas 14, 15. Area 14 becomes the huge thalamic mass of the human brain, while area 15 becomes the *subthalamus* (ventral thalamus). The position and relation of the subthalamic area are noteworthy. It is interposed between the thalamic above (14) and hypothalamic below (7, 8, 9), and between the striate area (6) in front and the tegmental areas (17) of the mid-brain behind, serving as a junctional centre for the masses developed from these areas.

The areas mapped in the mid-brain are: tegmental (18), supra-tegmental (16, 17), areas which become linked by the posterior commissure. Area 20 is the tectal area, the chief executive centre in the brain of the axolotl, while area 19 is involved in tectal functions. In area 21 we reach the cerebellar region of the hind-brain, while area 22 is the tegmental mass which occupies the region of the isthmus, the constriction which separates mid- from hind-brain. With this introduction we pass on to consider the rise of the human cerebrum in the next chapter.

NOTES AND REFERENCES

[1] A simile used by the late Sir G. Elliot-Smith.

[2] For recent literature on the development and evolution of the thalamus, see Kappers, Ariens, note [3], Chapter IX; Kuntz, A., *A Text Book of Neuro-Anatomy*, 1937; Herrick, C. Judson, *Jour. Comp. Neur.*, 1937, 67, 381; Clark, W. E. Le Gros, *Brain*, 1932, 55, 406; *Proc. Roy. Soc.*, 1937, 123 (B), 166; *Phil. Trans.*, 1935, 204, 313; *Jour. Anat.*, 1933, 67, 536 (med. geniculate bodies); *ibid.*, 1936, 71, 7 (tracts leading to); Clark and Russell, *ibid.*, 1939, 73, 255; Clark and Others, *Proc. Roy. Soc.*, 1939, 126 (B), 449 (visual pathways to); Clark, W. E. Le Gros, *Jour. Anat.*, 1941, 75, 419; *ibid.*, 1942, 75, 131 (structure of lat. geniculates); Glees and Clark, *ibid.*, 1941, 75, 295; Goldby, F., *ibid.*, 1941, 75, 197 (thalamus); *ibid.*, 1942, 75, 131 (projection of nuclei to cortex); *Med. Jour. Australia*, 1939, p. 4 (in chimpanzee); *ibid.*, 1937, 71, 103 (in dog); *J. W.*, *ibid.*, 1938, 69, 103 (in diencephalon).

[3] For recent literature on the hypothalamus, see *The Hypothalamus*, by W. E. Le Gros Clark, J. Beattie, G. Riddoch, and N. M. Dott, 1938. References to Ariens Kappers, Kuntz, and Herrick given in preceding note [2]; Clark, W. E. Le Gros; *Jour. Anat.*, 1936, 70, 203; Beattie, J., *ibid.*, 1937, 71, 151; Heslop, T. S., *Brit. Jour. Surg.*, 1938, 25, 884; Ries and Langworth, *Jour. Comp. Neur.*, 1938, 68, 22 (in whale); Scharrer, E., *Zeitsch. Anat. Entwickl.*, 1937, 106, 169.

[4] For an early statement of the animal functions situated in the hypothalamus, see Dr. Harvey Cushing's Lister lecture, *Lancet*, 1930, 2, 119, 175; *Proc. Nat. Acad. Sc.*, 1931, 17, 239.

[5] See p. 35, *The Hypothalamus* (reference in note [3]); Dart, Raymond, *Jour. Anat.*, 1935, 69, 3; Burkitt, A. N., *Proc. Linn. Soc. N.S.W.*, 1934, 59, 5.

[6] For some of the recent papers on the anatomy and development of the pituitary, see Atwell, J., *Proc. Ass. Res. for Nerv. and Ment. Dis.*, 1936, 17, 333; Frazer, J. E., *Manual of Embryology*, 1940; Nelson, W. O., *Amer. Jour. Anat.*, 1933, 52, 307 (of pig); Brander, F. J., *Proc. Roy. Soc. Med.*, 1936, 29, 609; Hair, C. W., *Anat. Rec.*, 1938, 71, 141 (nerve supply); Wade, H. J., *Jour. Anat.*, 1938, 72, 216 (pars intermedia); Shanklin, W. M., *ibid.*, 1940, 74, 459; 1944, 78, 79 (cells of the neural lobe); Lucas Keene and Hewer, *Lancet*, 1924, 2, 111 (secretion in foetal life); Phelps-Allis, E., *Jour. Anat.*, 1931, 65, 247 (evolution of).

[7] *The Brain, from Apes to Man*, 1928.

[8] Gilbert, Margaret S., *Anat. Rec.*, 1935, 62, 337.

[9] Cave, A. J. E., *Jour. Anat.*, 1931, 65, 364; Keith and Tweedie, *Proc. Roy. Soc. Med.*, 1911, 4, 47 (case of ectopia); Kingsbury and Roemer, *Amer. Jour. Anat.*, 1940, 66, 449 (pharyng. pituit. in dogs).

[10] Gaskell, W. H., *The Origin of Vertebrates*, 1908.

[11] Keith, Sir A., *Lancet*, 1911, 1, 993, 1002.

[12] Wislocki, G. B., *Amer. Jour. Anat.*, 1937, 61, 95; Schwartz, H. G., *Anat. Rec.*, 1937, 67, 35; Sunderland, S., *Jour. Anat.*, 1945, 79, 33.

[13] See Popa and Fielding, *Jour. Anat.*, 1930, 65, 88; 1933, 67, 227 (circulation of); see also Wislocki, G. B. (reference in preceding note); 'Epinasse, P. G., *Jour. Anat.*, 1934, 68, 11.

[14] Wislocki and King, *Amer. Jour. Anat.*, 1936, 58, 421; Mahoney and Sheehan, *Brain*, 1936, 59, 61; Gersh, I., *Anat. Rec.*, 1938, 70, 93 (suppl. 3); von Knobloch, D., *Zeitsch. Anat. Entwickl.*, 1937, 106, 379; Spiegel, E., *ibid.*, 1937, 106, 154.

[15] Krabbe, K., *Anat. Hefte*, 1916, 54, 191; Gladstone and Wakeley, *The Pineal Organ*, 1940; Levin, P. M., *Jour. Comp. Neur.*, 1938, 68, 405 (in rhesus monkey); Shafik, A., *Jour. Anat.*, 1939, 73, 419 (experimental).

[16] In fishes both parapineal and pineal (the posterior glandular body) are present. In amphibia the parapineal tends to disappear; in reptiles both structures are present; in mammals the parapineal is absent.

[17] Gladstone and Wakeley, see note [15].

[18] Clark, W. E. Le Gros, *Jour. Anat.*, 1940, 74, 471.

[19] Cooper, Eugenia, *Jour. Anat.*, 1932, 67, 28.

[20] Herrick, C. Judson, *Jour. Comp. Neur.*, 1937, 67, 381.

CHAPTER XI

THE FORE-BRAIN OR PROSENCEPHALON (continued) CEREBRAL VESICLES

We are now to follow the development of the organ which has given man the domination of the world—the cerebrum proper, comprising the right and left cerebral hemispheres. Nothing could be simpler than the cerebral vesicles at the end of the 1st month of development: they are merely button-like bulges on the right and left walls of the fore-brain (Fig. 121). Each button-like vesicle may be demarcated into three areas—a relatively small olfactory area in front, which will be evaginated to form the *olfactory vesicle*, afterwards converted into the olfactory bulb and tract; a *striate area*, in which that great basal mass of nerve nuclei known as the *corpus striatum* will be developed; and a *pallial* or *mantle* area, in which the cortical centres which make up the great mass of the cerebral hemispheres are produced. In each vesicle there is also a fourth or *secretory area*, which, however, does not become defined until the middle of the 2nd month, when it is folded within the cavity of the vesicle to form the glandular covering of the choroid plexus of the lateral ventricle.

It is important to note the manner in which the cerebral vesicles are connected to the walls of the 3rd ventricle and to each other. At what may be called its posterior border each vesicle is continuous with the optic thalamus (Figs. 121, 122); at its lower border, with the hypothalamic region. At both of these borders it is the striate area which joins with the thalamic regions; nerve tracts which arise in the nuclei of these regions and pass to the mantle must traverse the striate zone: there is no other route. Hence the corpus striatum becomes the bond which links each cerebral vesicle to the thalamencephalon; it becomes the highway for the *internal capsule*, the name given to the great afferent and efferent nerve-tracts which link the lower nerve centres to the cortex and the cortex to the lower centres.

Having thus examined the connections of the cerebral vesicles along their posterior and inferior borders, we now turn to the remaining two—the anterior and superior borders (Figs. 121, 122). Along the anterior border one cerebral vesicle is united to the other by the *lamina terminalis*, which, we shall see, becomes enormously distorted by the development within it of (i) the anterior commissure, (ii) the hippocampal commis-

sure, and (iii) on its immediate vicinity, the corpus callosum (see Figs. 144, 145, 146). Along the superior border the vesicles are united by a roof plate; posteriorly the cerebral roof plate is continuous with that of the 3rd ventricle, which at the 6th week becomes transformed into choroidal ependyma (Fig. 136). A similar change affects the roof plate and a neighbouring area of the cerebral wall to form the *velum interpositum*. The roof plate at first lies over the widely gaping orifice of the cavity of the cerebral vesicle (Fig. 121). By the end of the 6th week (Fig. 122) the expansion of the cerebral vesicles has commenced; we can then name the cavity of each vesicle—*lateral ventricle*; and its constricted communication with the 3rd ventricle, the interventricular opening or *foramen of Monro*.

Expansion of the Cerebral Vesicles.—By the middle of the 2nd month the rapid expansion of the cerebral vesicles has commenced, as may be

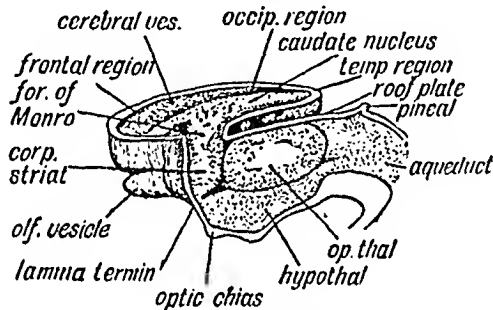


FIG. 134. The expansion of the right Cerebral Vesicle and the formation of the Corpus Striatum in its floor, during the 6th week of development.

seen in Fig. 134. Already the posterior or temporal region is passing backwards and downwards on the side and roof of the thalamencephalon (Fig. 135); the frontal region is bulging forwards over the olfactory bulb, while the roof of the vesicle, which is cut away in Fig. 134 to expose the corpus striatum in the floor, is rising up so that between the right and left vesicles there now exists a fissure—the commencement of the *longitudinal fissure*, which will become deeper and longer as the vesicles expand. We have already seen that the striate area of each vesicle is continuous with the thalamic area of the fore-brain, and thus as the corpus striatum becomes differentiated it is continuous with the optic thalamus (Fig. 134), and hence this striate thalamic junction may be looked on as the stalk or hilum from which the cerebral expansion takes place. The corpus striatum occupies the floor of the vesicle, so that in the fully formed brain we find the caudate nucleus stretching along the lateral ventricle from the foramen of Monro to the end of the descending horn which represents the posterior or caudal pole of the embryonic brain.

It is also instructive to note the expansion of the cerebral vesicle as seen on its lateral aspect (Fig. 135). At the 6th week the bean-shaped vesicle still leaves the greater part of the thalamencephalon exposed; it then shows only a frontal and temporal pole, but by the end of the 3rd month the expansion has reached the mesencephalon, and now there has appeared a third or occipital pole (Fig. 135, *B*); by the end of the 5th month the occipital region overlaps and covers the hind-brain. On embryological grounds alone one could infer that the dominance of the cerebrum is one of the more recent products of evolution. In the lateral aspect we again see how the corpus striatum forms the basis or fixed area from which the cerebral expansion is produced. The three primary

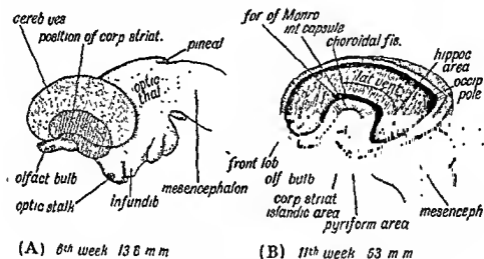


FIG 135. The expansion of the left Cerebral Vesicle as seen on its lateral aspect. *A*, at the 6th week; *B*, at the 11th week. In *B*, a window has been cut to expose the lateral ventricle, the corpus striatum and the choroidal gap (After Illis)

constituents of the cerebral vesicle are indicated in Fig. 135, *A*: the small olfactory area, the large mantle formation and the position of the striate element at the junction of these two. The position of the corpus striatum determines the non-expansion of the overlying cortex—which later becomes differentiated to form the Island of Reil. The position and relationships of the islandic region towards the end of the 3rd month are shown in Fig. 135, *B*.

The Velum Interpositum.—It is during the growth backwards of the cerebral hemispheres over the thalamencephalon that the basis of that complex structure the velum interpositum is formed. The basis of this structure is really that area of the pia mater, the mesodermal [1] and vascular capsule of the brain, which is enclosed between the thalamencephalon and expanding cerebral vesicles (Fig. 136). The essential parts of the velum are its lateral edges, which project within

the lateral ventricles and its lower surface lying over the 3rd ventricle—parts which are covered by reflections of those areas of the neural tube which have been converted into a glandular or secretory epithelium. These parts form the choroidal villi—or plexuses—covered by the ependymal epithelium, which secrete cerebro-spinal fluid.

We have seen that in the anterior part of the roof plate of the 4th ventricle the cerebellum is developed, while its posterior half becomes the

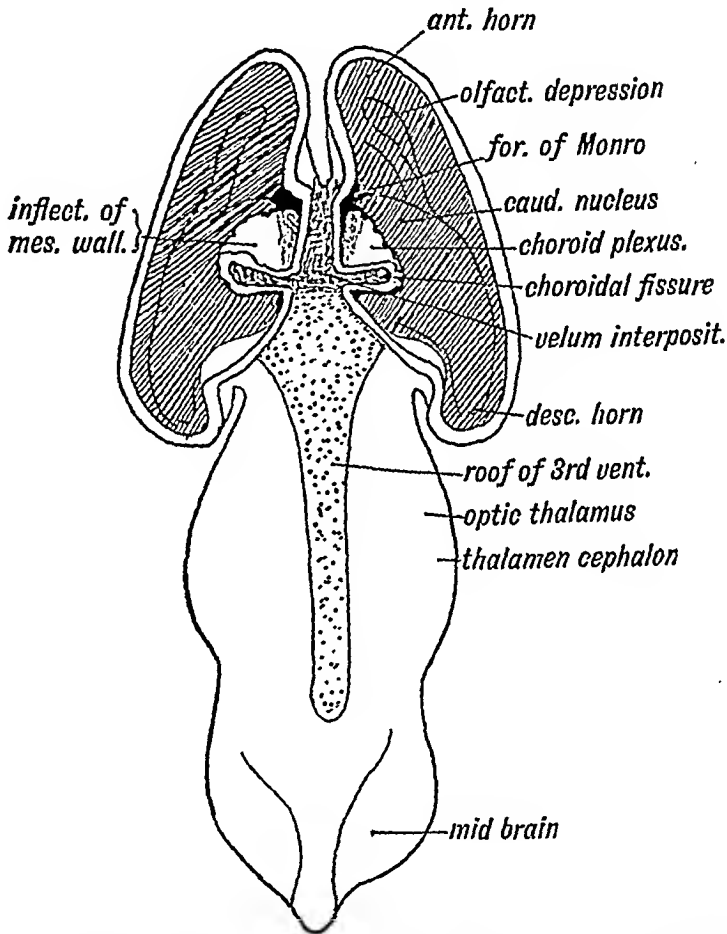


FIG. 136. A dorsal view of the Fore- and Mid-Brain in the 6th week of development to show the formation of the Velum Interpositum. The cerebral vesicles are laid open and the inflection of the roof of the fore-brain shown on the ingrowing velum. The roof plate of the 3rd ventricle is also exposed. (Modified from His.)

inferior medullary velum—a secretory membrane (Fig. 108, p. 140). The roof plate of the 3rd ventricle, from the foramina of Monro backwards to the stalk of the pineal body, becomes modified in a similar manner (Fig. 136). It forms merely the ependymal covering of the lower surface of the velum interpositum, thus clothing the choroid plexus on the roof of the 3rd ventricle (Fig. 137). The anterior part of the roof plate protrudes within the cerebral vesicles at the foramina of Monro, and covers the apex of the velum interpositum (Fig. 136). The

mesial wall of each cerebral vesicle from the foramen of Monro to the posterior extremity of the vesicle (Figs. 135, 137), which becomes the tip of the descending horn, is also inflected and forms a secretory ependyma, covering the velum interpositum and choroid plexus within the lateral ventricles. Into this inflection—the *choroidal fissure* of the embryonic neural wall—springs the mesoderm, carrying vessels with it. The velum interpositum is thus composed of a basis of mesoderm [1], while its intraventricular parts have an ependymal covering derived from the neural wall. When the velum interpositum is withdrawn from the foetal brain (Fig. 135, B) a linear opening is seen extending from the foramen of Monro to the temporal end of the cerebral vesicle.

The choroid plexus, which merely fringes the velum in the adult, completely fills the cavities of the embryonic lateral ventricles. These for the first three months are relatively very large and their containing walls thin. The velum and choroid plexus must play an important part in the development of the cerebral vesicle in the early period of growth. The spread of the vesicles backwards and downwards over the optic thalami obscures the original simple relationship of the velum to the brain; but, when withdrawn from the transverse fissure, the velum is seen to rest on the optic thalami and project within the ventricle from the foramen of Monro to the tip of the descending horn. This stretch marks the line at which the choroidal inflection took place. The *taenia semicircularis* (*stria terminalis*), in the groove between the optic thalamus and caudate nucleus (Fig. 127), marks the line at which the mesial wall of the cerebral vesicle was primarily attached.

The fibrous substance of the velum interpositum is continuous with the pial covering of the brain, and also with the edge of the tentorium cerebelli, for as the cerebral vesicles expand not only do they evaginate their proper mesodermal covering, the pia-arachnoid, but also the inner or dural stratum of the primitive cranial capsule. The corpus callosum and cerebral vesicles, as they develop, grow backwards and enclose, between the optic thalami below and the pillars of the fornix above, the fibrous basis of the velum interpositum. The veins of Galen are developed in the velum and join the straight sinus in the tentorium.

Corpus Striatum.—When a coronal section is made of the adult brain (Fig. 137) to expose the connections of the velum interpositum, it is clear that a mere overgrowth of the cerebral vesicles will not account for all the relationships shown. We shall see that the development of the commissures—particularly of the fornix and corpus callosum—introduces elements not seen in the simple brain of the embryo; but, besides the commissural, another change has come about in the relationship of the corpus striatum to the optic thalamus. So intimate and extensive has

the union between them become that the corpus striatum now forms a cap upon the lateral aspect of the optic thalamus (Fig. 137). Although developed in the wall of the cerebral vesicle, the lenticular nucleus of the corpus striatum and the islandic cortex are now constituents of the lateral wall of the 3rd ventricle—the cavity of the original thalamencephalon. The intimate union of the corpus striatum with the optic thalamus we must regard as the result of two developmental processes: the formation of the nerve tracts of the internal capsule—which begin to appear in the 3rd month—and the neurobiotactic attraction which exists between the neuroblastic centres of the two great basal ganglia.

Two figures (Figs. 138, *A*, *B*) by the late Sir G. Elliot-Smith throw

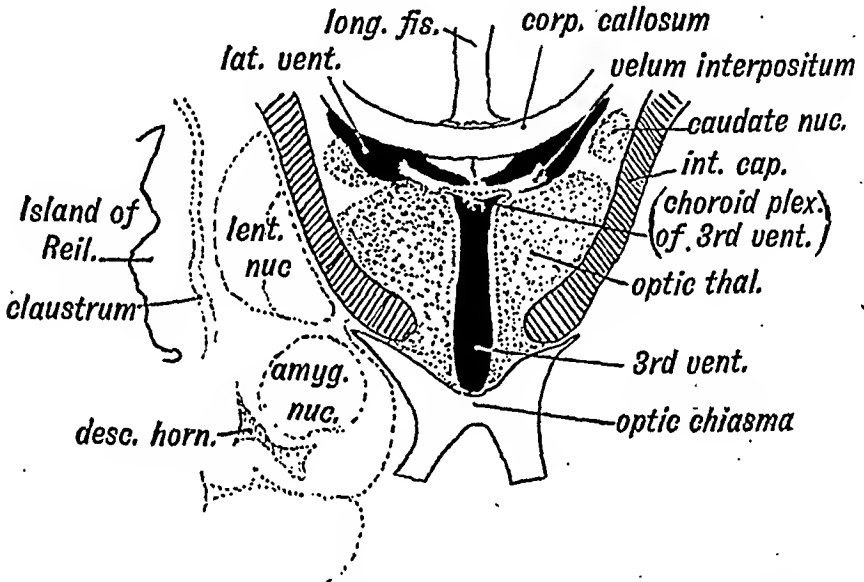


FIG. 137. Diagrammatic section across the 3rd and Lateral Ventricles of the Adult to show the structures formed in their walls.

light on the nature and origin of that complex product of the cerebral vesicle, the corpus striatum [2]. When the cerebral hemisphere of a turtle's brain is laid open, as in Fig. 138, *A*, we see the same three elementary parts as in the cerebral vesicle of the human embryo: (i) the hollow olfactory bulb, containing an extension of the ventricular cavity; (ii) a mass occupying the floor and lateral wall, representing the corpus striatum; (iii) the vesicular wall, mantle or pallium. We see that the basal mass is made up of three projections: (i) the hypopallium or neostriatum, representing the greater part of the caudate nucleus and also the outer part of the lenticular nucleus—the putamen; (ii) at its hinder or temporal end the amygdaloid nucleus; (iii) the oldest part of all, lying over the olfactory bulb (Fig. 138, *A*) and continuous with the hypothalamic region—the palaeostriate body. The

palaeostriate body is represented by the deepest part of the human lenticular nucleus—the nucleus pallidum. From Fig. 138, *A*, it is clear that the corpus striatum has a close connection with the olfactory region of the cerebral vesicle and also with the hypothalamus (Fig. 134). The coronal section in Fig. 138, *B*, shows the relationship of the corpus striatum to the remaining parts of the wall of the cerebral vesicle of a primitive mammal—the type of organ from which the human cerebrum has been evolved. An artery—the lateral striate [3], one of the perforating branches of the anterior cerebral—is seen to enter the wall of the brain between the pyriform lobe above and the olfactory tubercle below and end in the corpus striatum. On the medial wall of the ventricle (Fig. 138, *B*) an elevation marks the *hippocampus*; it arises as an ingrowth or inflexion of the mantle, the hippocampal fissure marking the

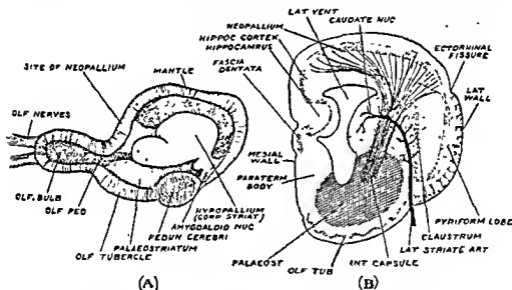


FIG. 139.

- A.* Sagittal section of Turtle's Cerebral Vesicle made along the mesial plane so as to expose the cavity of the vesicle—the lateral ventricle. The hypopallium is the same as the neo-striatum. (Elliot-Smith)
- B.* Coronal section of a Primitive Mammalian Cerebrum, made across its anterior part, in front of the 3rd ventricle, to show the origin of the constituents of the corpus striatum. The part marked "claustrum" also includes the putamen of the neo-striatum. (Elliot-Smith)

line of the infolding. Elliot-Smith regarded the corpus striatum as a derivative of the cortex. In the brain of the hird neuroblasts, which are cortical in nature, grow inwards, thus tending to fill up the ventricular cavity. Nevertheless we must regard the corpus striatum as being functionally different from the cortex or mantle.

The history of the basal ganglia of the human brain is epitomized by Dr. Abbie in Fig. 139, *A*, *B*. In Fig. 139, *A*, we see how closely the nuclei of the striate body, derived from the telencephalon, have become

associated with those of the thalamus, developed in the wall of the thalamencephalon. The parts evolved from the old striate of the smell brain are represented by the globus pallidus and medial nucleus of the amygdaloid; these are separated from the receptive centres of the thalamus by the internal capsule (Fig. 139, *A*). It will also be seen that the internal capsule separates the new striate into putamen and caudate nucleus (*caud. n.*). The claustrum is also part of the putamen separated by the development of the external capsule (Fig. 139, *A*).

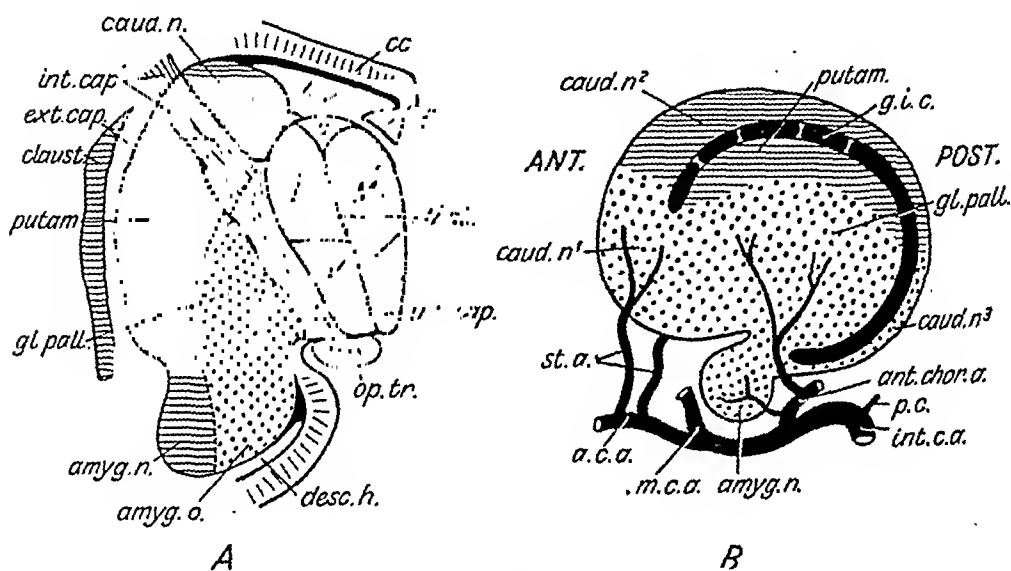


FIG. 139.

A. Coronal section of the Basal Ganglia of the Human Brain. (After Abbie.)

cc, corpus callosum; *f*, fornix; *l.v.*, lateral ventricle; *thal.*, thalamus (fine stippling); *a*, anterior nucleus; *M*, mesial nucleus; *L*, lateral nucleus; *V*, ventral nucleus; *int. cap.*, internal capsule; *ext. cap.*, external capsule; *op. tr.*, optic tract; *desc. h.*, descending horn; *amygd. o.*, old amygdaloid nucleus; *amygd. n.*, new amygdaloid; *gl. pall.*, globus pallidus; *putam.*, putamen; *claustr.*, claustrum.

B. Sagittal section of Basal Ganglia of the right half of an Ape's Brain, viewed on their mesial aspect. (After Abbie.) The parts derived from the paleostriatum are coarsely stippled; those which form part of the neostriatum are shaded horizontally.

caud. n¹, part of head of caudate nucleus and of putamen derived from the paleostriatum; *caud. n²*, part of caudate nucleus derived from the neostriatum; *putam.*, part of putamen (neostriate) which rises above the level of the globus pallidus; *g.i.c.*, gateway for internal capsule; *gl. pall.*, globus pallidus; *caud. n³*, tail of caudate nucleus derived from paleostriatum; *amygd. n.*, new part of amygdaloid nucleus; *int. c. a.*, internal carotid artery; *p.c.*, posterior communicating branch; *ant. chor. a.*, anterior choroidal artery; *m.c.a.*, middle cerebral artery; *a.c.a.*, anterior cerebral artery; *st. a.*, striate branches.

Another aspect of the striate body is shown in Fig. 139, *B*. Coarse stippling marks out the older parts, which include the globus pallidus, the amygdaloid, and tail of the caudate. Part of the head of the caudate and part of the putamen are also paleostriate in origin. The blood supply to the paleostriatum is depicted in Fig. 139, *B*; it is remarkable for its constancy [3].

Thus the corpus striatum has two stages in its evolution. The older elements came into being when the cerebral part of the brain was mainly

olfactory in function, as in fishes and amphibia. These older elements, the paleostriatum, have to do with the co-ordination of fundamental movements such as affect the whole body (swimming), or are concerned in basal functions such as feeding, copulation, etc. This older stage of evolution we may speak of as the *pre-cortical*. With the evolution of the cerebral cortex (pallium) came the development of the neostriatum, which has to do with the co-ordination of movements initiated in the cortex, movements usually described as voluntary. This newer stage in evolution we may speak of as the *cortical* stage.

The Mantle or Pallium.—We have followed the fate of the striate body of the embryonic cerebral vesicle; the differentiation of the olfactory area will be dealt with when we come to consider the nose and sense of smell; there remains for consideration the third or pallial area of the cerebral vesicle. Even up to the end of the 3rd month the pallial wall of the vesicle remains thin; it then measures only about 1 mm. in thickness. Originally the pallial wall shows the same three strata or zones as were seen in other parts of the neural tube—namely an inner or ependymal zone, in which neuroblasts are produced; a middle or mantle zone, in which they are differentiated; and an outer or marginal zone (Fig. 140). In the spinal cord the masses of neuroblasts were differen-

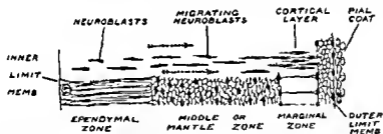


FIG. 140. Diagram to show the differentiation of the Pallial Wall of the Cerebral Vesicle. (After His)

tiated within the middle zone, where they remained; but in the cerebellum—and the same is true of the pallial wall—they invade the marginal zone. It is within the neuroglial scaffolding of the marginal zone that the grey cortical matter of the cerebral hemispheres is formed. In the 2nd month the migration of the neuroblasts to form a cortical layer has already commenced; the process is particularly active in the 3rd and 4th months. Not only is there a migration from the ependymal to the marginal layer, but the production is particularly abundant where the mantle joins the corpus striatum. The middle zone, which contains grey matter in the spinal cord, is here the highway for the fibres developed from the cortical cells; it forms the white medullary mass of the cerebral hemispheres.

Evolution of the Neopallium.—Nothing could be more humble than the origin of man's master organ: it was evolved in connection with the sense of smell. The cerebral hemispheres, as we know them in the lowest vertebrates, are for the reception and interpretation of impulses from the olfactory end organs. Connections are established between the olfactory brain and the motor centres in the cord and in the hind- and mid-brain; olfactory impressions can thus lead to action. Further, it became advantageous that there should be a nervous mechanism for the blending of impressions from the nose with impulses derived from sight, hearing and touch, and hence there arose connecting tracts by which stimuli streaming in from the various senses could be combined and their reactions co-ordinated with those streaming in from the nose. In the stem of vertebrates which became mammalian the supreme co-ordinating mechanism was evolved in that part of the neural system connected with smell—the telencephalon [5].

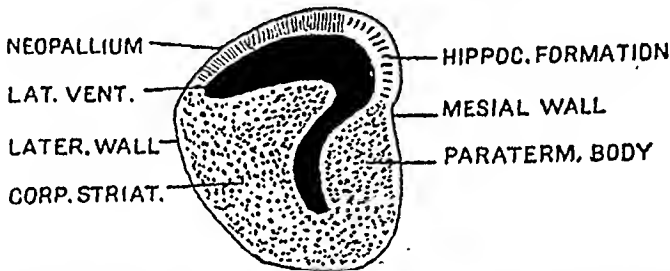


FIG. 141. Section across the Left Hemisphere of a primitive vertebrate Brain anterior to the Lamina Terminalis, to show the small extent of the neopallium and the relatively great development of the corpus striatum and rhinencephalon. (After Elliot-Smith.)

In Fig. 141 is represented a diagrammatic section across the anterior part of the cerebral vesicle of one of the lower vertebrate types—such a one as we may suppose preceded the modern mammalian form of cerebral hemisphere. There is a cavity within it—the lateral ventricle. The inner or mesial wall is formed of two parts: (i) the hippocampus or hippocampal formation—true cerebral cortex or mantle; (ii) below the hippocampus, the paraterminal body—a nuclear mass connected with the hippocampal formation by nerve tracts. The lateral or outer wall of the primitive hemisphere is made up of two parts: (i) the corpus striatum, a nuclear mass partly covered by the cortex of (ii)—the pyriform lobe (see Fig. 138, B). The pyriform lobe receives fibres from the lateral root of the olfactory tract. These four parts—hippocampus, paraterminal body, pyriform lobe, corpus striatum—are connected with smell, and form the primitive mantle (archipallium) of the brain. In the roof of the ventricle an expansion of the mantle appears between the hippocampal formation on the inner side and the pyriform lobe on the outer side (Fig. 141); to

this expansion Elliot-Smith, whose account is followed here, gave the name of neopallium [6]. It is this new mantle which becomes the basis for higher combination of the sensory impressions coming in from all the organs of sense. It becomes the seat of consciousness and memory, and in man assumes enormous proportions; hence the great and rapid expansion of the cerebral vesicles in the human foetus.

As may be seen from Fig. 146, the primitive mantle—all the cortical formation directly connected with the sense of smell—is arranged around the peduncular attachment, which may be described as the cerebral hilum. In Fig. 147 is shown how greatly the distribution of the primitive mantle is altered when the great commissures become developed.

Projection Fibres to the Neopallium.—A transverse section of a mammalian brain of a primitive type—made further back and in a more

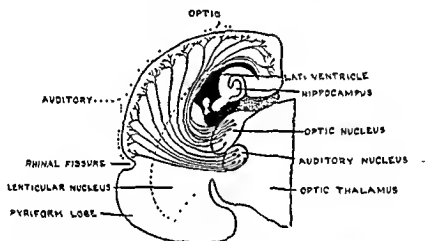


FIG 142 Coronal section of the right half of the Cerebral Vesicle of a Primitive Type of Mammal, showing the termination, in the neopallium, of projection fibres which arise in the optic thalamus (Elliot-Smith)

advanced stage of development than that represented in Fig. 141—is shown in Fig. 142. The section illustrates the manner in which projection fibres, arising from nuclei in the optic thalamus and connected with the sense of sight and of hearing, spread outwards into the neopallium—each set streaming into the area which lies nearest to it. In this way the mantle of the telencephalon becomes a higher sensorium for the reception, blending and storing of all sensory impressions. Other illustrations of the cortical afferent tracts are given in Figs. 123 and 138, B.

Localization of Function in the Neopallium.—In Fig. 143 the brain of a primitive mammal is represented on its lateral aspect. The major part is seen to be made up of pyriform lobe, olfactory bulb and tubercle, all of them parts of the rhinencephalon. The rhinal fissure marks the

junction of the neopallium with the older parts of the mantle on the outer or lateral aspect of the hemisphere. The areas adjacent to the various nuclei of the optic thalamus receive projection fibres from these nuclei. Thus it comes about that the lower and most posterior part of

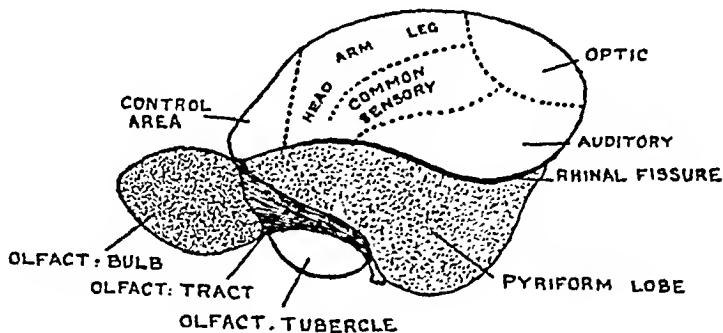


FIG. 143. Lateral aspect of the Cerebrum of a Primitive Mammal to show the rhinal fissure, which separates the neopallium above from the older parts of the mantle below, represented by the pyriform lobe. The areas of the neopallium in which the projection tracts from the optic thalami terminate are also shown. (Elliot-Smith.)

the neopallium, which forms the basis of the temporal lobe, receives fibres from the auditory centre; in the upper posterior part the fibres from the optic nuclei end; this area becomes the main part of the occipital lobe. Anterior to these two areas terminate the projection

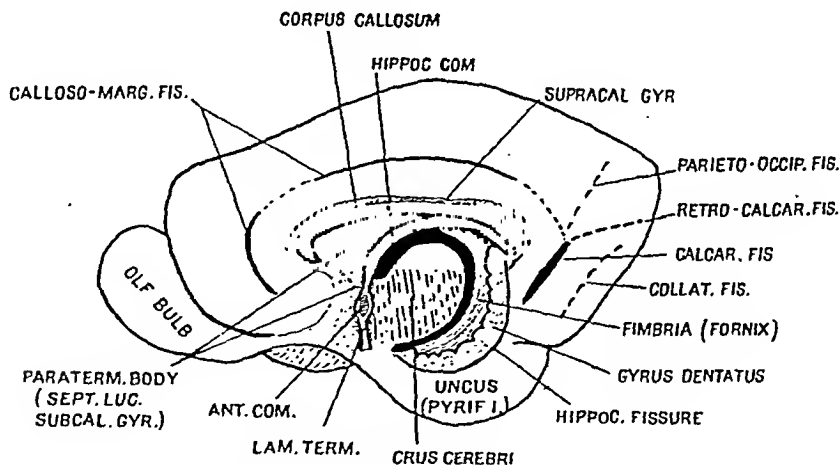


FIG. 144. The Anterior, Hippocampal and Callosal Commissures, with the primary fissure on the mesial aspect of a typical mammalian cerebrum. (Elliot-Smith.)

fibres connected with the sensory nuclei of the Vth nerve and with the nuclei of common sensation—receiving impulses from the leg, trunk, arm and head [7]. Hence the surface areas of the body are represented in the neopallium. Naturally it is in connection with this area, the area of common sensation, that the cortical fibres which control the lower somatic motor nuclei arise. Anterior to the motor areas—occupy-

ing the region of the frontal pole—is an area connected with the control of the higher centres [6]. These are the primary areas of the neopallium. In the course of evolution, secondary or associated zones have appeared

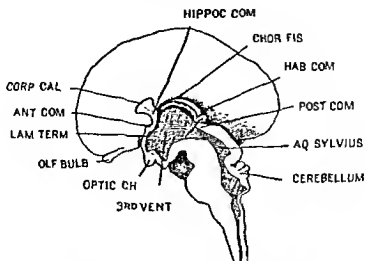


FIG. 145. Mesial aspect of the Brain of a Human Fetus in 4th month of development, showing the lamina terminalis and positions at which commissures are formed.

round the primary areas, separating them widely and giving rise to the great mass of the human cerebrum.

Development of Cerebral Commissures.—In order to secure a co-ordinated action of the whole brain, it is necessary not only that the

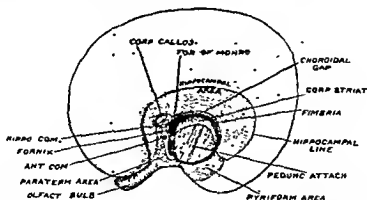


FIG. 146. Mesial Aspect of the Cerebral Vesicle of a Fetus about 3 months old, showing the commissures developing in the lamina terminalis and the distribution of the cortical areas which belong to the rhinencephalon. (After Streeter.)

cerebral centres of each hemisphere should be linked up by association and projection fibres, but that the centres of one hemisphere should be united by transverse or commissural tracts with the corresponding centres of the other hemisphere. The lamina terminalis (see Figs. 122, 145, 146) affords a natural bridge for the formation and passage of the

commissures. In the most primitive vertebrates, in all of which the cerebral hemispheres are chiefly olfactory in nature, the anterior commissure is already present. The next to appear is a dorsal or hippocampal commissure, which unites the hippocampal areas on the mesial surfaces of the cerebrum (Figs. 144, 146). The last and greatest to be formed is the corpus callosum; it appears in the true mammals—not in monotremes and marsupials. Its development is commensurate with the size of the neopallium; hence it is largest in man.

The cerebral hemispheres are thus connected by fibres which cross in the lamina terminalis, and form three main commissures. (i) The *anterior* or *ventral commissure*, which connects the olfactory bulbs, olfactory tubercles, the pyriform lobes and amygdaloids—in brief, all the primary parts of the smell brain; (ii) the *dorsal* or *hippocampal* commissure, also formed in the lamina terminalis: in man this commissure becomes the fornix; (iii) the *corpus callosum*, which unites the neopallium of one side with that of the other. It is formed at the upper limit of the lamina terminalis above the dorsal or hippocampal commissure (Figs. 144, 145, 146). The *middle* or *grey commissure* in man (Fig. 127) is an adhesion between the ependymal coverings of the optic thalami; the *optic chiasma* (p. 158), the *habenular* or *superior commissure* (p. 168) need only be again mentioned. The *posterior commissure* is formed in the roof plate at the junction of the mid- and fore-brain (Figs. 119, 127).

(i) *The Anterior Commissure* is developed in the lamina terminalis—the primitive anterior wall of the fore-brain. The commissure crosses in the lamina terminalis below and rather anterior to the foramen of Monro.

(ii) *Hippocampal Commissure*.—Four parts are recognized in the fornix of the human brain (Fig. 147): (i) the body, adherent to the under surface of the corpus callosum; (ii) the posterior pillars, which are continuous with (iii) the fimbriae and fibres of the alveus, covering the ventricular aspect of the hippocampus; (iv) the anterior pillars, which end in the corpora mamillaria, where hippocampal impulses are relayed to the anterior nuclei of the thalamus and to the tectum. The fornix contains two systems of fibres: (i) those which cross and connect the hippocampal cortex of one side with that of the other, and form the true dorsal or hippocampal commissure (psalterium or lyra); (ii) fibres which connect the various parts of the rhinencephalon of the same side with each other, and with the epithalamus, hypothalamus, corpora mamillaria and thalamus.

To understand the development of this system it is necessary to obtain a clear conception of the relationships of the lamina terminalis to the various parts which have been distinguished in the rhinencephalon

(Figs. 144, 146). On each side the lamina terminalis is continuous with the *paraterminal body* or area—that part of the rhinencephalon which lies immediately in front of the lamina terminalis. The paraterminal body becomes the subcallosal gyrus and septum lucidum in the mature brain (Fig. 147). The hippocampal formation, which includes the hippocampus and fascia dentata, bounds the choroidal fissure above. Fibres developed in the hippocampal formation cross to the opposite side in the lamina terminalis above the anterior or ventral commissure, thus forming the *dorsal* or *hippocampal commissure* (Fig. 145). It becomes included in the body of the fornix. The posterior pillar is developed in the hippocampal cortex, which forms the lip of the choroidal fissure. The anterior pillar lies in the paraterminal body, lamina terminalis and hypothalamus.

(iii) *Corpus Callosum*.—The corpus callosum is the commissure of

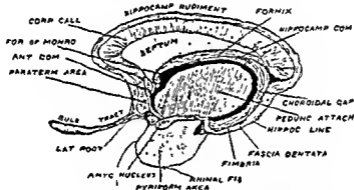


FIG. 147 Diagram to show the structures formed in the Lamina Terminalis and Primitive Callosal Gyrus. (After Elliot-Smith)

the *neopallium*, and hence in man, in whom the neopallium forms by far the greatest part of the cerebrum, this commissure attains an enormous development. The commissural fibres begin to form towards the end of the 3rd month, crossing in the lamina terminalis dorsal to the fibres of the hippocampal commissure (Figs. 145, 146). As the corpus callosum increases rapidly during the 3rd and 4th months, forming the genu in front and the splenium behind, the adjacent field of hippocampal cortex becomes widely attenuated and separated. Under the genu is the subcallosal gyrus, made up from the paraterminal body and from the hippocampal cortex. The splenium, as it develops, presses the main hippocampal formation down and back, until it reaches its permanent position [8]. The backward expansion of the corpus callosum brings about a stretching of the hippocampal commissure, the body and anterior pillars of the fornix being thus shaped. The velum interpositum is overwhelmed and buried during the growth backwards of the corpus

callosum and fornix. The paraterminal body is stretched to form the septum lucidum and subcallosal gyrus. Thus by the development of the corpus callosum those two parts of the rhinencephalon, the paraterminal body and hippocampal formation, originally in close union, become widely separated. The supracallosal and subcallosal gyri with the striae longitudinales are vestiges of their former union. The corpus callosum may not be developed—a rare occurrence; it is remarkable that this condition cannot be detected during the life of the individual [9]. The cavity within the septum lucidum is formed during the development of the corpus callosum [10].

Formation of Convolutions.—Until the 5th month the surface of the cerebral vesicle is comparatively smooth. Till then the three strata of the cerebral vesicle, the ependymal layer within, the cortical or nerve-cell layer on the surface and the medullary or nerve-fibre layer between, have increased at an equal rate. In the 6th and 7th months certain areas of the cortex increase rapidly, the increase affecting the superficial strata to a very much greater extent than the deep, and affecting the cortex much more than the medulla, with the result that the surface of the cerebrum becomes raised into certain definite eminences or gyri, separated by depressions or fissures. The chief fissures are already well differentiated in the foetus of the 7th month; during the last two months of intrauterine development the secondary and tertiary sulci appear. The process of fissuration and convolution-formation is thus practically finished at birth. In the spinal cord the tracts of nerve fibres are formed outside the masses of grey matter; in the cerebral vesicle the tracts are formed beneath the grey matter—between the grey matter and the ependyma (see p. 181). The neuroblasts in the cortex have reached nearly their full number by the 7th month; after then it is their dendrites and collateral fibres that continue to develop (His).

Development of the Cortex.—The mantle or wall of the cerebral vesicle of the brain becomes differentiated into a thin outer grey layer or cortex, containing the nerve cells, and an inner deep stratum—the medulla—of great thickness and made up of nerve fibres and tracts associated with the nerve cells of the cortex. The cortex is the substratum of consciousness, memory and mind. It is educable; it is the seat of skill. We naturally expect the great mental development which takes place in the earlier years of life to be accompanied by a corresponding change in the microscopic structure of the cortex. There is such a change, but it is difficult to measure for two reasons: (i) every area of cortex has its own peculiar structure and thickness; Elliot-Smith distinguished 28 areas in the cortex, each having its own peculiar structure; (ii) Dr. Joseph Bolton observed that in some cases a newly born child may show

a more mature development than a child of 3 months, there being as much variation in structure of cortex as in degree of ability. The latter observer noted that the cortex began to laminate or divide into strata of nerve cells in the 5th month; it is then that the mother becomes conscious of foetal movements. Soon after the 5th month gyri and fissures begin to form on the lateral surface of the brain, for as we shall see later, fissures appear on the mesial surface at a still earlier date. Dr. Bolton also made the important observation that the outer or pyramidal (supra-granular) stratum was the latest in growth, and that the great development of this layer is the characteristic of the human cortex [11].

Supragranular Cortex [12].—By the end of the 6th month the foetal

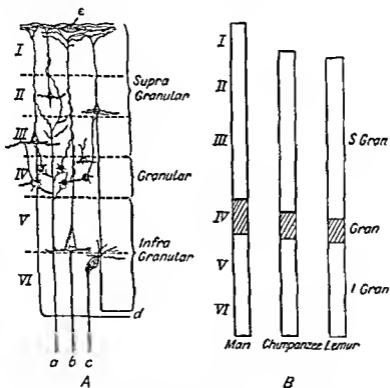


FIG 148

A A diagrammatic representation of the chief cellular elements in the Cortical Strata of the Adult Brain. The strata are numbered I–VI from the surface inwards (After Kuntz)

a, afferent fibre terminating around cells of stratum IV (inner granular cells), and also around cells of the supra granular strata (I, II, III); b, c, efferent fibres from pyramidal cells of V, and from a polymorphic cell in VI; d, association fibre from an outer granular cell of stratum II; e, a zonal cell in the superficial or plexiform stratum, I.

B Three columns representing the thickness of the Cerebral Cortex of Man, Chimpanzee, and Lemur. The granular stratum is shaded. The relative development of the supra granular and infra granular strata may thus be estimated. (After van't Hoff)

cortex has become delaminated into six strata, numbered I–VI by Rodman, No. I being the plexiform, superficial stratum and VI the deepest or polymorphic. In Fig. 148 is given a diagrammatic repre-

sentation of the chief cellular constituents of the strata of the adult cortex. From an evolutionary point of view, the three deeper strata (*IV*, *V*, *VI*) are the older; they are represented in the cortex of the reptilian brain. The granular cells of *IV* are receptive; round them terminate incoming fibres carrying impulses from stations in the thalamus, and olfactory nuclei (Fig. 148, *A*, *a*). The granular cells deliver their charges to the effector cells, the inner pyramidal and polymorphic cells in strata *V*, *VI*; efferent fibres from these cells proceed to effector centres in the base of the brain, in the brain stem and in the spinal cord (Fig. 148, *A*, *b*, *c*). Superficial to the granular stratum come the three supragranular (*I*, *II*, *III*), in which lie the receptive and analytical powers of the cortex. The supragranular cortex reaches its highest development in the human brain (Fig. 148, *B*). It is also the last to reach full development in the human brain, complete differentiation not being reached until the 5th year. In the precentral or motor cortex, stratum *IV* is almost lacking, whereas in sensory areas, such as the postcentral, occipital and temporal regions, stratum *IV* is thickly studded with granular cells. The supragranular strata of the human brain are richer in pyramidal cells than are those of the chimpanzee [13], although in actual depth of cortex the difference between the two is not great (Fig. 148, *B*).

The Principal Fissures.—The principal fissures of the brain are: (i) those connected with the rhinencephalon—namely the hippocampal fissure, which appears on the mesial aspect of the cerebral hemisphere before the end of the 2nd month [14]; it limits or bounds the hippocampal gyrus (see Fig. 146, hippocampal line); also the rhinal fissure, which appears later (Figs. 143, 147); (ii) those connected with the isolation of the Island of Reil—the fissure of Sylvius, the superior, inferior and anterior limiting fissures; (iii) those in the occipital cortex connected with the sense of sight—the calcarine, retro-calcarine, lunate sulcus (Affenspalte), parieto-occipital and collateral; (iv) the callosomarginal of uncertain import; (v) the central fissure or fissure of Rolando, which is formed between motor and sensory areas of the cortex; (vi) the orbital; (vii) the sulcus rectus; (viii) the intra-parietal; (ix) the 1st temporal or parallel, which partially demarcates the auditory cortex [15]. In the 7th month the fissures on the human brain have a remarkable correspondence to those on the cerebrum of an ape (Figs. 149, 151). We have already seen that the so-called *choroidal fissure* is formed by an inflection of the cerebral wall to form the choroidal villi of the lateral ventricles (Fig. 136).

Significance of Convolution.—There is some circumstance which limits the thickness of the cortex. If the cortical cells increase in number,

accommodation is obtained not by adding to the thickness of the cortex but by enlarging the superficial area of the cerebrum. The cortex is correlated in its extent with the bulk of the body and with the area of the integumentary covering. Hence large animals such as whales and elephants have much convoluted brains. The rich convolutions of man's brain may be in some degree related to the nude and sensitive skin of his body (Elliot-Smith). The most satisfactory explanation of the number and arrangement of the convolutions of the human brain is to be found in a study of the evolution of its various functional areas. The cortex was originally composed of primary sensory areas—connected with sight, touch, hearing, smell, etc. When secondary and higher zones were produced in connection with the primary areas, the surface of the brain was necessarily thrown into folds and fissures to provide the increase of surface required. Hence we find that the principal

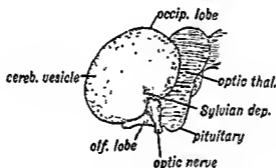


FIG. 149 Lateral aspect of the Cerebral Hemisphere at the end of the 2nd month.

fissures are related to certain cortical areas. Elliot-Smith distinguished three kinds of fissures: (i) those like the calcarine and central fissures which separate one cortical area from another (being *limiting* fissures or sulci); (ii) those like the lunate (Fig. 156), where the line of cortical demarcation lies not at the bottom of the fissure, as in the last, but at the brink of the fissure. These are named *operculate*, because the convolution or operculum which causes the fissure or depression arises at the junction of two areas; (iii) a developing area may fold inwards, thus giving rise to a depression in the centre of an area, like the retro-calcarine in the midst of the visuo-sensory area (Fig. 157). The hippocampal linear depression and Sylvian fossa, as we have already seen (pp. 175, 179), are peculiar in their formation. Three fissures—the calcarine, collateral and hippocampal—actually cause an infolding of the whole thickness of the mantle, and give rise to elevations in the posterior and descending horns of the lateral ventricle.

Formation of the Island of Reil and Fissure of Sylvius.—When the lateral wall of the cerebral vesicle is examined at the 5th month (Fig.

150) an area of cortex is seen to be becoming submerged by the upgrowth of the surrounding cortex. The submerged area is the Island of Reil; it covers that part of the wall of the cerebral vesicle which is thickened by the corpus striatum (Figs. 135, *B*, 137), the islandic area becoming larger as the basal ganglia grow in mass and in importance. The climax of this development is reached in the human brain. The submerged area becomes triangular in shape, the apex being directed backwards; it is bounded by three limiting *sulci*—an anterior, superior and inferior. The rising lips of cortex, which bound the limiting *sulci*, form the temporal, fronto-parietal and orbital opercula, and ultimately meet over the submerged area (Fig. 152). The fissure of Sylvius separates the opercula. It will be readily grasped that the development of the

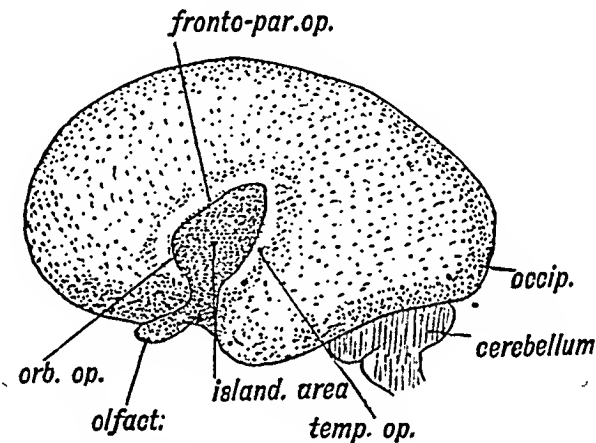


FIG. 150. The same aspect during the 5th month.

corpus striatum prevents the expansion of the insular part of the vesicle, whereas the thin-walled mantle out of which the other lobes of the brain are developed expands readily and overwhelms the thickened area. The corpus striatum begins to form during the 2nd month, hence as early as that date the insular depression is visible on the lateral wall of the hemisphere (Fig. 149). This mechanical explanation of the origin of the fissure of Sylvius is probably only partially true; the relatively great growth of the cortex which forms the opercula is due in the main to the importance of the functions lodged in the opercula. By comparing Figs. 149 and 151, it will be realized that the formation of the Sylvian fossa is connected with the expansion and rotation of the temporal lobe in a forward and downward direction. The growth of the temporal lobe and the differentiation of the occipital pole (see Fig. 150) give the impression that there has been an actual rotation downwards of the cerebral vesicle on the Island of Reil. The lower end of the stem of the Sylvian fissure also indents the rhinencephalon, separating the

uncinate gyrus from the anterior parts of the rhinencephalon (Figs. 147, 150).

The student is already familiar with the fact that the Island of Reil forms a cortical cap to the corpus striatum. The structures between the islandic cortex and the foramen of Monro represent a section of the thickened wall of the cerebral vesicle (Fig. 137). Convolutions appear on it in the 6th month, when the rest of the cortex also begins to become convoluted. Further, the larger the area of cerebral cortex in any primate, the larger is the Island of Reil; the more convoluted the cortex, the more convoluted the Island. Flechsig has shown that the cortex of the Island is joined to all the cortical areas of the mantle by bands of association fibres. Hence the Island must be regarded as playing a

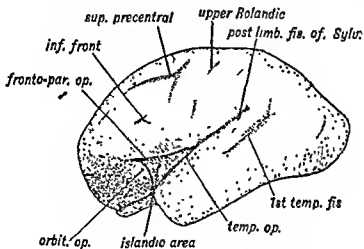


FIG 151. The same aspect during the 7th month.

highly important part in co-ordinating the functions of the brain [16].

The Opercula.—Three opercula grow up and cover the Island of Reil (see Figs. 151 and 152): (i) the temporal, (ii) the fronto-parietal, (iii) the orbital. The late Prof. D. J. Cunningham [17] found that during the later months (7th–9th) of foetal life an opercular part, known as the *pars triangularis* (Fig. 152, B) appeared in quite 50% of brains and was more frequently present on the left side than on the right, probably owing to the dominant centres for speech being situated on the left side. The *pars triangularis* is the anterior part of the upper or dorsal operculum (labelled fronto-parietal in Figs. 150, 151, 152), the anterior horizontal limb of the fissure of Sylvius being the continuation of the upper limiting sulcus of the Island of Reil. The *pars triangularis* is cut off from the dorsal operculum by the formation of the ascending limb of the fissure of Sylvius (Fig. 152, B). The temporal operculum rises first (5th month), the others a month later. The opercula which

153) the fronto-orbital fissure has been labelled *ant. lim. sulcus*, as if it were identically the same as the anterior limiting sulcus of the human brain. The same system of identification has been applied to the chimpanzee brain in Fig. 154, *A*. The identification of the fronto-orbital fissure with the anterior limiting sulcus of the Island of Reil seems to be confirmed by the condition shown in Fig. 154, *B*, where the Island is limited in front by the fronto-orbital fissure. This is true of the anthropoid brain, but not of the human, for in human brains the anterior limiting sulcus and the fronto-orbital fissure maintain a separate existence. The true orbital operculum, then, lies behind the fronto-orbital fissure, not in front of it, as in Fig. 154, *B*.

Calloso-Marginal Fissure.—This fissure on the mesial aspect of the brain arises from the fusion of the genual and intercalary fissures of the typical mammalian brain (Fig. 144). Its origin is probably the result of a pressure due to the growth of the cortex surrounding the corpus callosum, for if that structure be absent, the usual form of this fissure is completely altered. It separates one set of cortical areas from another (Elliot-Smith).

Calcarine and Correlated Fissures [19].—In the typical mammalian brain the calcarine fissure forms part of the same arcuate system as the genual and intercalary (Fig. 144). The part of the cerebral wall in which it is formed encloses the posterior horn of the lateral ventricle (Fig. 270, *B*, p. 318). The cortex on the lower or posterior lip of the fissure shows the stria of Gennari, which characterizes the cortex in which the optic radiations end. The calcarine fissure is thus a limiting fissure formed between striate and non-striate cortex. The *retro-calcarine fissure* or depression, which continues the calcarine sulcus backwards to the occipital pole, is formed by the growth and involution of the striate cortex (Fig. 157). In the ape's brain the striate cortex on the lateral aspect of the occipital pole increases rapidly and rises up as a lip or operculum over the cortex of the parietal lobe. The depression in front of the operculum is known as the *simian fissure* (Affenspalte) or *sulcus lunatus* (Fig. 153). In the human brain the great increase of the parietal cortex, a seat of association centres, has pushed the sulcus lunatus almost to the occipital pole (Fig. 156), or it may, especially in the more civilized races, be completely obliterated [20]. Further, the Y-shaped occipital sulcus (external calcarine) on the lateral aspect of the occipital pole (Figs. 153, 156) may join the retro-calcarine sulcus. Sir G. Elliot-Smith distinguished not only the striate area, in which the optic radiations end, but two surrounding areas, an outer zone—the peristriate—and an intermediate—between the outer zone and the striate area. Certain sulci have arisen in connection with the evolution

of these two association or visuo-psychic areas. The *collateral fissure* below the calcarine (Fig. 157) probably results from a mechanical pressure exercised by the growth of the striate area. The *parieto-occipital fossa* or depression on the mesial aspect of the brain results from the inflection of an area of cortex between the calcarine areas of growth behind and the area of association centres on the mesial aspect of the parietal lobe in front (Fig. 157). The production of the parieto-occipital fossa, with its complex of buried convolutions and sulci, is also related to the growth backwards of the corpus callosum. In human

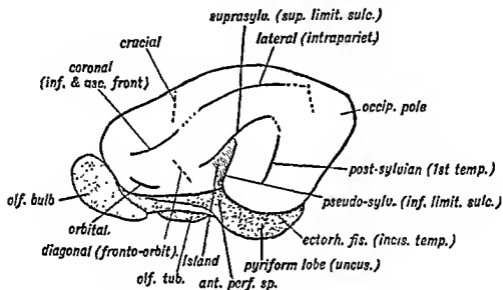


FIG. 155.
Smith
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brains where this structure is absent the buried convolutions and sulci are superficial.

Orbital Fissure.—This fissure is present in most mammalian brains, but its significance is still doubtful.

Fissure of Rolando, or Central Fissure, appears during the 6th month as an upper and lower linear depression, which join together in the course of development (Fig. 151). The fissure appears between the motor (agranular) areas of cortex in front of it, and the sensory (granular) areas behind it, and is therefore a limiting fissure. The upper part does not quite correspond to the crucial sulcus of the brain of the cat and dog, for in them that sulcus forms the *anterior* limit of the motor areas (Elliot-Smith) (Fig. 155); the lower segment may represent part of the coronal fissure. The fissure of Rolando reaches its fullest development in man; it is found only in the higher primates (monkeys and anthropoids).

The **Inferior Frontal Fissure** appears before the fissure of Rolando and occurs in primate brains in which that of Rolando is not developed. It seems older than the fissure of Rolando. In the brains of all Old World monkeys the inferior frontal fissure is made up of two parts, a bent or arcuate fissure, with the straight fissure immediately in front of it (Fig. 153). It is not easy to identify these two fissures in either the anthropoid or human brain. The most likely interpretation is to regard the inferior frontal of man as derived from the lower half of the arcuate fissure, while the middle frontal of human anatomy corresponds to the upper half of the arcuate of the monkey's brain. In the evolution of the human brain there have been great additions to the cortex in the

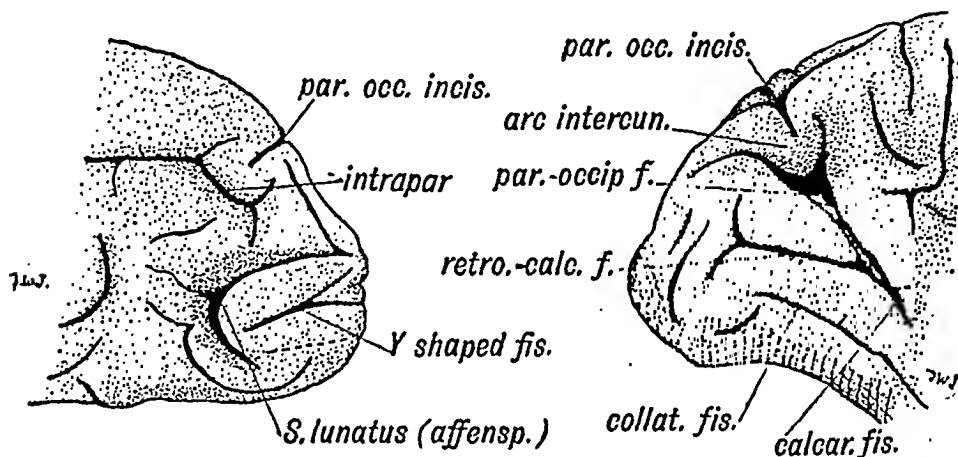


FIG. 156.

FIG. 157.

FIG. 156. The lateral aspect of the Occipital Lobe of a Human Brain, showing the sulcus lunatus (Affenspalte). (Elliot-Smith.)

FIG. 157. The mesial aspect of the Occipital Lobe of a Human Brain, showing the complex nature of the parieto-occipital fissure. (Elliot-Smith.)

region of the arcuate fissure, with the result that, in the human brain, the representative of the straight fissure is found pushed towards the frontal pole [21].

Intra-parietal Fissure.—The intra-parietal fissure appears between three areas of growth: (i) the cortex of the inferior parietal lobule below, chiefly consisting of association areas related to the visual and auditory and perhaps also to the areas of common sensation; (ii) the occipital cortex posteriorly; (iii) the cortex behind the fissure of Rolando. It corresponds to the lateral fissure of the cat's brain (Fig. 155), while the whole of the intra-parietal fissure of the ape's brain (Fig. 153) may be regarded as equivalent to the ascending rami in the human brain (Jefferson). The ascending, horizontal and occipital limbs of this fissure arise independently in connection with separate

areas. They may or may not become conjoined. All the parts of the fissure are limiting in nature [22].

Parallel or First Temporal Fissure [23].—The first temporal fissure separates the first temporal gyrus, in which the auditory centres are situated, from the neighbouring cortex (Figs. 153, 155). As the first temporal gyrus rises to form the inferior operculum of the Island of Reil, part of it, in the form of a number of gyri which connect it with the Island, is huried in the fissure of Sylvius. In these deep gyri Campbell located the terminations of the auditory tracts, the superficial part of the first temporal convolution forming association areas for the auditory centre (Fig. 292). The first temporal fissure corresponds to the post-Sylvian fissure of the typical mammalian brain (Fig. 155).

Secondary Sulci and Gyri.—During the 8th and 9th months the

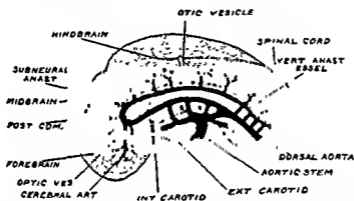


FIG. 158. Diagrammatic representation of the Arteries of the Brain at the end of the 1st month of development. (After Prof. H. M. Evans)

remaining sulci and convolutions of the brain are formed. For the greater part these are peculiar to the human brain.

Vessels of the Brain.—The embryonic arteries from which the cerebral and vertebral arteries become evolved are shown in Fig. 158. The dorsal aorta, in which the aortic arches end, is continued forward to the fore-brain, where at the root of the optic vesicle and near the site of the future vallecule of Sylvius it divides into anterior and posterior branches; the anterior branches will become the stem of the middle and anterior cerebral arteries as the cerebral vesicles begin to expand, while the posterior branch becomes continuous with the subneural anastomotic vessel, from which the posterior communicating and basilar arteries will become differentiated and from which the posterior cerebral will arise. The subneural anastomotic chain is fed by segmental vertebral branches of the dorsal aorta (Fig. 158). From this segmental network are formed the vertebral arteries. The right and left anastomotic vessels

as the cerebral vesicles grow back their veins are transferred first from the primitive vein to the cerebellar and then to the venous system of the hind-brain. From the anastomotic channel thus opened up are fashioned the transverse and sigmoid sinus. In the foetal brain the Island of Reil is enclosed by a venous circle. From this anastomotic chain veins ascend to the longitudinal sinus, while others descend to the cavernous sinus [27].

During later foetal development lacunae are formed in the frontal, parietal and occipital segments of the longitudinal sinus. In the 2nd year villi or granulations are developed within these lacunae, forming Pacchionian bodies, thus providing for drainage of the cerebro-spinal fluid.

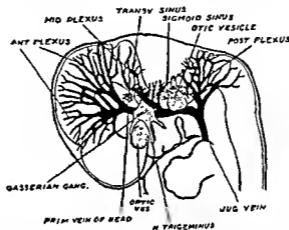


FIG. 159. The Primitive Vein of the Head and its tributaries in the 6th week of development, with indications of the new anastomotic channels opened up during the 3rd and 4th months (After Streeter.)

Membranes of the Brain.—Even before the cephalic part of the neural tube is enclosed, mesodermal (mesenchymal) cells spread in between it and the surrounding mesoderm, thus supplying a primitive covering for the tube. Out of the covering become differentiated: (i) the pia-arachnoid and its vessels; (ii) the membranous cranial capsule, from which in turn are separated (a) the dura mater, (b) enclosing bones and pericranium, and (c) the connective tissues of the scalp. It is probable that the tissues of the pia-arachnoid are derived in part, if not wholly, from the neural crest of the medullary plates of the cephalic region [28]. The differentiation of the membranes of the brain and spinal cord is closely related to the establishment of a *cerebro-spinal fluid system*. We have seen (p. 139) that the choroid plexuses of the ventricles of the brain become developed in the 7th week, when the human embryo is about 15 mm. long. Dr. L. H. Weed found that at this stage of development in the pig, the cerebro-spinal fluid formed in the 4th ventricle began to

fuse under the hind-brain during the 6th week to form the basilar artery [24].

The brain is at first covered by a capillary plexus out of which the main arterial and venous channels are fashioned. The anterior cerebral artery has been evolved from the plexus covering the medial aspect of the olfactory brain and the middle cerebral from the lateral olfactory vessel (Abbie). The posterior cerebral originally sprang from the posterior division of the internal carotid ; in higher primates its origin has been transferred to the basilar artery [25].

Arterial Distribution.—Prof. Joseph Shellshear has, in a series of researches on the distribution of arteries in the brain, brought forward evidence to prove that nuclei or areas of cortex which serve a separate function have their own arterial supply. Arteries tend to be limited in their distribution to definite functional areas. For instance, the arterial supply to the paleostriatum remains the same from the lowest to the highest vertebrate brain (Abbie). Further, in the evolution of the mammalian brain, arteries have remained wonderfully constant in their distribution, so that a fissure may be identified by noting the artery which enters it [26].

The embryological basis out of which the *venous sinuses* and cerebral veins are developed is shown in Fig. 159. At the middle of the 2nd month the veins of the fore- and mid-brain unite behind the stalk of the optic vesicle to form the *primitive vein of the head*, which, passing backwards internal to the Gasserian ganglion, leaves the interior of the cranial cavity in front of the ear to become the primitive jugular or anterior cardinal vein. Before leaving the interior of the skull it receives a cerebellar venous trunk (mid-plexus, Fig. 159) and after its exit a medullary trunk (post-plexus, Fig. 159)—which escapes by the jugular foramen. With the expansion backwards of the cerebral vesicles during the 3rd, 4th and 5th months the system of the longitudinal and transverse sinuses becomes evolved by the union of the venous networks included in the longitudinal fissure between the cerebral vesicles and between the cerebral vesicles and cerebellum. The main changes are indicated in Fig. 159 ; only part of the primitive vein persists—the part lying internal to the Gasserian ganglion that becomes the *cavernous sinus* ; the extra-cranial part of the primitive jugular disappears towards the end of the 2nd month, but it occasionally persists as an emissary vein emerging at the root of the zygomatic process. Two important anastomotic channels open up (Fig. 159) : (i) the pre-cerebellar, which drains the tributaries of the fore- and mid-brain into the primitive cerebellar trunk ; (ii) the post-cerebellar, which unites the cerebellar trunk with the veins of the hind-brain ; the hind-brain trunk escapes by the jugular foramen. Thus,

most medial centres of the thalamus, which receive sensory tracts from the face, lips, and tongue, end in the lowest or most lateral areas of the post-central cortex. The representation of the body in the neocortex is thus inverted.

[8] Dr. Abbie (*Jour. Comp. Neur.*, 1939, 70, 9) has reinvestigated the development and evolution of the corpus callosum and finds that it is not developed in the hippocampal formation, as Elliot-Smith had observed, but immediately above that formation. Prof. F. Goldby has re-examined the evidence and confirms the accuracy of Elliot-Smith's account (*Jour. Anat.*, 1940, 74, 227).

[9] Many accounts of non-development of the corpus callosum in the human brain have been published. For a report of a case of partial absence, see Drennan, G. R., *South African Med. Jour.*, 1935, 9, 625; Dr. L. S. King (*Jour. Comp. Neur.*, 1936, 64, 337) reports on a breed of mice in which defects of the corpus callosum are hereditary.

[10] Thompson, J. M., *Jour. Anat.*, 1932, 67, 59; Beyers and Dart, *ibid.*, 1925, 59, 358.

[11] For literature on the development and evolution of the neopallial cortex, see Bolton, Joseph, *Brain*, 1919, 32, 26; *Henderson Trust Lectures*, No. 12, 1933

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Cerebral Atlas, 1938; Wood-Jones, F., *The Matrix of the Mind*, 1928; Woodlard, H. H., *Jour. Anat.*, 1931, 65, 224; von Bonin, G., "Evolution and Significance of the Cerebral Cortex," *Illinois Monographs*, 1945, 5, No. 3; Glees, P., *Jour. Anat.*, 1944, 78, 47 (cortico-striate connections); Stern, K., *ibid.*, 1942, 76, 302 (thalamo-frontal connections); Verhaart and Kennard, *ibid.*, 1949, 74, 239 (inhibition area); Goldby, F., *ibid.*, 1939, 73, 599 (in Echidna); *ibid.*, 1949, 74, 12 (in phalanger); Sunderland, S., *ibid.*, 1949, 74, 201; *The Post-natal Development of the Human Cerebral Cortex*, 1939, by J. Le Roy Conel.

[12] For evolution of cerebral cortex, see references given in preceding notes [6], [11], and also Hesdorfer and Scammon, *Anat. Rec.*, 1935, 64, 443 (growth of cortex and basal ganglia); Abbie, A. A., *Med. Jour. Australia*, 1939, p. 421 (cortex as seat of emotions); *Australian Jour. Exper. Biol.*, 1938, 16, 143 (cortex of monotremes); Agduhr, E., *Anat. Rec.*, 1941, 89, 191 (criticism of von Economo's estimate of number of cortical neurons).

[13] Kreht, A., *Zeitsch. Anat. Entwickl.*, 1936, 195, 676.

[14] See references under note [4].

[15] Shellshear, J., *Jour. Anat.*, 1927, 61, 215.

[16] For racial variations in Island of Reil and opercula, see Levin, G., *Amer. Jour. Phys. Anthropol.*, 1937, 22, 345; Grzybowski, J., *Archiv. d'Anat.*, 1938, 25, 115.

[17] *Jour. Anat.*, 1890, 24, 127; see also reference to G. Levin in preceding note.

[18] For discussion of the nature of the anterior limiting sulcus of the Island of Reil, see Keith, Sir A., *Researches in Prehistoric Gahlee*, 1927.

[19] For literature on the development and evolution of the visual cortex, see u, E., *Archiv. d'Anat.*, 19. i., Ngowyang, G., *Jour. Co and Sunderland, Jour. Ar*, 75, 225 (anatomical evidence supports the Young-Helmholtz theory); Sir G. Elliot-Smith's first paper on the visual cortex appeared in *Jour. Anat.*, 1907, 41, 193.

[20] Shellshear, J., see under preceding note [19].

escape through a localized area in the inferior medullary velum and to collect in the overlying mesodermal tissue [29]. At the site of escape an opening is formed in the medullary velum, the *foramen of Majendie* arising in this way. The foramen formed in each lateral recess of the 4th ventricle is produced in a similar manner. The subarachnoid spaces thus commence over the 4th ventricle and round the medulla oblongata, and from the region of the hind-brain the system extends proximally and distally until, by the middle of the 3rd month of development, the entire neural space is enclosed by the arachnoid. The mesodermal condensation which bounds the subarachnoid system becomes the arachnoid; the pia mater represents the subarachnoid tissue. At the same time as the subarachnoid spaces are being formed another plane of cleavage sets in external to the arachnoid, the arachnoid being thus separated from the dural layer of the cranial capsule and a potential space produced—the *subdural*. These spaces, particularly the subarachnoid, do not represent parts of the lymphatic system; lymphatic vessels, we shall see, arise like blood vessels; nor does the cerebro-spinal fluid represent a species of lymph.

NOTES AND REFERENCES

[1] I use the term "mesodermal," but "neurodermal." would be more apt, for it is almost certain that the pia mater is derived from the neural crest.

[2] For evolution of corpus striatum, see Elliot-Smith, Sir G., *Jour. Anat.*, 1919, 53, 271; Ariëns Kappers, see note [3], Chapter IX; Dart, R. A., *Jour. Anat.*, 1935, 69, 3; Herrick, C. Judson, *An Introduction to Neurology*, 1931; Abbie, A. A., *Jour. Anat.*, 1934, 68, 433 (blood-supply); Shaner, R. F., *Jour. Comp. Neur.*, 1936, 64, 213 (in pig); Durward, A., *Jour. Anat.*, 1934, 68, 492 (in sparrow); Goldby, F., *ibid.*, 1934, 68, 159 (in lizard); Landau, E., *Archiv. d'Anat.*, 1936, 23, 167 (origin of claustrum); Schepers, G. W. H., *Jour. Anat.*, 1938, 72, 535 (brain of tortoise).

[3] For vascular supply of basal ganglia, see Shellshear, J., *Jour. Anat.*, 1921, 55, 27; Abbie, A. A., see under preceding note [2].

[4] For the nature of the hippocampal infolding, see Abbie, A. A., *Jour. Comp. Neur.*, 1938, 68, 307; Hines, M., *ibid.*, 1922, 34, 73.

[5] For evolution of the neopallium, see Elliot-Smith, Sir G., *Lancet*, 1910, 1, 147, 221; Ariëns Kappers, see reference, note [3], Chapter IX; Herrick, C. Judson, *Brains of Rats and Men*, 1926; see also reference in preceding note [2]; Wood-Jones, F., *The Matrix of the Mind*, 1928; Tilney, F., *The Brain from Ape to Man*, 1928.

[6] Prof. Raymond Dart has sought for the origin of the mammalian neocortex in certain cortical formations he has distinguished in the brains of reptiles (*Jour. Anat.*, 1935, 69, 31).

[7] The projection of tracts from thalamus to cortex takes place in a definite order. Those from the most lateral aspect of the thalamus, its ventral nucleus, which receives sensory fibres from the lower limbs and lower part of the trunk, are projected to the upper or most medial areas of the cerebral cortex. The

CHAPTER XII

THE CRANIUM

Natural Divisions of the Skull.—The human skull is the product of many long epochs, during which it has undergone great changes, but we have every reason for supposing that its general functions have remained much the same since the vertebrate form of animal was evolved. In the first place it has to form a brain-case—a neuro-cranium. Man's brain has reached a degree of development which rendered great changes necessary in this part of the skull. In the second place, the skull has to shelter and protect the special organs of sense—the ear (temporal bone), the eyes (orbits), the olfactory area (nasal region), and taste (bucco-pharyngeal region). In the third place, the skull forms an essential part of the structures concerned in mastication: the facial part of the skull is in reality a scaffolding for the palate and teeth. In the main the facial part of the skull is visceral or splanchnic in function, and hence is sometimes spoken of as the splanchno-cranium. The outstanding characters of the human skull are the great size of the neuro-cranium and the small size of the splanchno-cranium.

Certain Phases in the Evolution of the Skull.—The skull has also been closely related to the function of respiration. In fishes the visceral skeleton of the skull forms the arches which carry the gills. We have seen that the representatives of these arches make a temporary appearance in the head of the human embryo. When a pulmonary replaced a branchial system a nasal airway was separated from the mouth by the formation of a primitive palate, such a palate as is seen in amphibians, reptiles and birds. With the evolution of chewing teeth in the mammalian stock the complete palate was formed, thus allowing the mammalian young to suck and the adult to chew and breathe freely at the same time. We see all of these stages manifested in the development of the human skull [1].

Cartilaginous Skull.—In trying to interpret the meaning of many of the developmental processes which we see taking place in the human embryo, it is often profitable to seek light from comparative anatomy, and no group of the lower vertebrates can help us in this respect so well as the selachians—the group of cartilaginous fishes to which sharks, rays and dog-fish belong. This is particularly true of the *chondrocranium*—the cartilaginous skull seen in the human foetus during the 2nd month

[21] For discussion on the homologics of frontal fissures, see Genna, G. E., *Revista di Antrop.*, 1924, 26, 1; Connolly, C. J., *Amer. Jour. Phys. Anthrop.*, 1936, 21, 306; von Bonin, G., *Jour. Comp. Neur.*, 1938, 69, 181; Shellshear, J., *Jour. Anat.*, 1939, 73, 327.

[22] Jefferson, G., *Jour. Anat.*, 1913, 47, 365.

[23] Shellshear, J., see under preceding note [15].

[24] Streeter, G. L., *Contrib. Emb.*, 1918, 8, 5.

[25] Abbie, A. A., *Jour. Anat.*, 1934, 68, 433 (history of cerebral arteries); Hughes, A. F. W., *Phil. Trans.*, 1934, 224 (B), 75 (development in brain of chick); Watts, J. W., *Jour. Anat.*, 1934, 68, 534 (fusion of anterior cerebral arteries in primates); Hochstetter, F., *Zeitsch. Anat. Entwickl.*, 1937, 107, 632 (termination of anterior basilar artery); Schepers, G. W. H., *Jour. Anat.*, 1939, 73, 451 (cerebral arteries of tortoise).

[26] See Shellshear, J., *Jour. Anat.*, 1931, 65, 45; *Proc. Roy. Acad. Sc. Amsterdam*, 1933, 36, 700; Abbie, A. A., *Brain*, 1933, 56, 233; *Jour. Anat.*, 1933, 67, 491; Sunderland, S., *ibid.*, 1939, 73, 120 (arterial supply of cerebral cortex and medulla).

[27] For development of cerebral veins and sinuses, see O'Connell, J. E. A., *Brain*, 1934, 57, 495; Boyd, G. I., *Jour. Anat.*, 1935, 69, 113 (frequency of emissary veins); Gibbs, E. and F., *Anat. Rec.*, 1934, 59, 419 (variations in lateral sinuses); Watt, J. C., *Anat. Rec.*, 1937, 67, 62 (suppl.).

[28] See Burr and Harvey, *Archiv. Neur. Psychiat.*, 1926, 15, 545.

[29] Weed, L. H., *Contrib. Emb.*, 1917, 5, 3; *ibid.*, 1920, 9, 425; Gladstone and Dunlop, *Jour. Anat.*, 1927, 61, 360; see also references given in note [5], Chapter IX.

these two terminal areas lies a large intermediate part which is definitely demarcated into two regions—orbital and otic (Fig. 163). Lying on the otic area and attached to it is the primitive maxillary apparatus—the tympano-hyal (Fig. 163), which corresponds to the stapes; the quadrate part of the palato-quadrate, which has been shaped in mammals to form the incus; and the upper end of the primitive mandible, which gives rise to the malleus—all lying exposed just as in the human embryo. On their appearance the incus and malleus are superficial in position; it is not until the human foetus has reached the 10th week of development that they become covered by the formation of the squamous plate of the temporal. The cartilaginous prominence—named post-orbital in Fig. 163, because it bounds posteriorly the orbital region of the primitive skull—is worthy of note because it represents the point at which a new mandibular joint, the *temporo-mandibular*, becomes evolved in mammals, and thus sets free the old maxillary parts for the service of the ear. The post-orbital process of the primitive skull becomes the site of the articular eminence in the mammalian skull, while the pre-orbital is represented by the internal angular process of the mammalian orbit. Thus, out of the primitive orbital region is fashioned not only the orbit but the whole floor of the temporal fossa, the malar bone and zygomatic arch being later formations evolved out of membranous skeletal elements. Similarly in the skull of the human embryo as in that of the shark, there are no cartilaginous representatives of the maxilla or premaxilla.

Growth of the Cranial Cavity.—The neuro-eranium is framed by the disposition of its bones and sutures so as to allow a free and easy expansion of the brain. By a mechanism we do not fully understand the bones entering into the formation of the cranial cavity grow as demand is made on them by the brain; at least, this is so in early life. When the cranial bones begin to form in the latter part of the 2nd month, the brain (cerebral vesicles) is only half an inch long—from frontal to occipital pole; in the adult the length is fourteen times as much and its volume fifteen hundred times larger. As the cerebral vesicles expand the developing bones alter in shape. By the 7th month of foetal life the relative proportions become approximately fixed [3]. During the first four years of life, brain and cranial growth go on rapidly. At birth the brain has attained from 20 to 22% of its size; by the 4th year over 80% of the volume is already present. There is a steady increase until the 18th or 20th year, when the brain attains its maximum volume—this, for the average Englishman, being about 1480 c.c.; after then there is a decline in the capacity of the cranium. The changes in the cranial walls are secondary to those in the brain [4].

develops. A glance at Fig. 162 will show why the roof must be fashioned from plastic material, for during the 3rd, 4th and 5th months the cerebral vesicles, lying over the prechordal region of the base, expand upwards and backwards until their occipital poles reach the tectal plates.

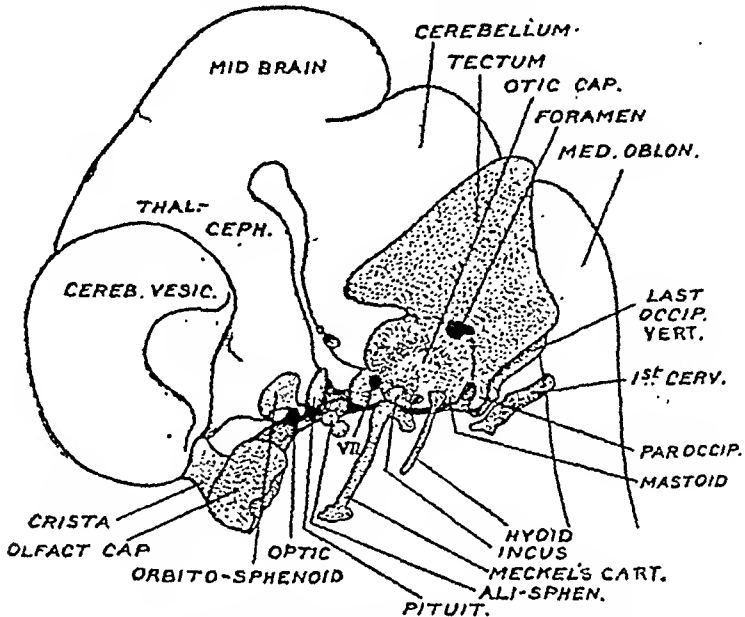


FIG. 162. Chondrocranium of a Human Embryo in the 8th week of development, seen from the side. (After Warren Lewis.)

There are certain other features seen in the lateral aspect of the foetal chondrocranium which call for comment here. The auditory capsule, the auditory ossicles and the region of the tympanum, save for their covering of soft parts, lie exposed on the surface of the skull. If we

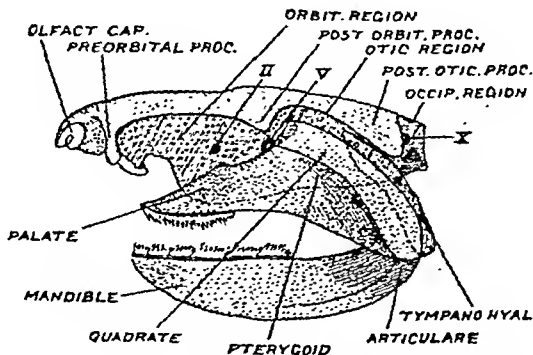


FIG. 163. Lateral aspect of Skull of Shark. (After Gegenbaur.)

turn to the lateral aspect of the cartilaginous skull of a shark we obtain an evolutionary explanation of this arrangement. At the anterior end (Fig. 163) is seen the nasal or ethmoidal region; the hind end is formed by the occipital area—compounded out of occipital vertebrae. Between

cord. As in the case of the cord the mesoderm grows under and over the cephalic part of the neural canal, and forms for it a *mesenchymal* or membranous covering. The covering of mesoderm thus formed is the primitive *Anlage* or foundation of the skull and of the brain membranes in the embryo.

Membrane and Cartilage Bones.—Only the base of the human skull is developed in cartilage, the rest is developed in membrane. How has such a condition arisen? The brain of *Amphioxus*, if it can be said to possess one, is wrapped in a membranous covering. In fishes with cartilaginous skeletons this embryonic mesodermal capsule becomes chondrified—plates of cartilage develop in it. As in the spinal column, the process of chondrification begins at the base and spreads slowly round to the crown or dorsum of the head. The cartilaginous cranium is an advance on the membranous stage. In many fishes a further most important element is added. The *dermal* bony plates, to which the placoid scales are fixed, become applied to the cartilage over the sides and dorsum of the skull. Thus to the cartilaginous element of the skull is added a third element—bone formed in membrane. Now, in the mammalian skull, and especially in that of man, the cerebral vesicles grow so quickly that long before the process of chondrification has had time to spread in the membranous capsule from the base to the crown, the dermal bones have formed, and thus supplant the cartilage on the calvarium. Hence, in the human skull, while the process of chondrification occurs in the base, and afterwards undergoes ossification, the roof and sides (calvaria) of the skull are formed by bones which, historically, are *dermal bones*, and hence are formed directly in membrane. The dermal bones of the human skull are: (i) the frontal, (ii) the parietal, (iii) the inter-parietal part of the occipital (the part above the superior curved lines), (iv) the squamous part of the temporal.

Thus the calvarial part of the skull passes directly from the membranous to the bony stage, while the base of the skull, like the spinal column, passes through three stages: (i) membranous, (ii) cartilaginous, (iii) bony. It will be thus seen that the base of the skull, developed in cartilage, is the most ancient part, while the dermal bones which form the calvaria represent later additions.

Development of the Calvarial (membranous or dermal) Part of the Skull.—In the 8th and 9th weeks of foetal life—the foetus being then about 25 mm. (1 in.) long—there appear on each side of the membranous cranial capsule four centres of ossification: (i) for the frontal bone, at a point just above the orbital margin and below the site of the frontal eminence (Fig. 165); (ii) for the parietal, at the position of the parietal eminence; this centre is double or even triple in nature, but the separate

From Fig. 164 it will be apparent that the walls of the cranium are made up of two very different parts—basilar and capsular. The basilar part is thick and developed in a cartilaginous basis. Growth proceeds as in a long bone; the lines between the basi-occipital and basi-sphenoid, the basi- and pre-sphenoid, and between the pre-sphenoid and ethmoid are growth or epiphyseal discs. The growth of the base of the skull is determined as much by the needs of the splanchno-cranium as by those of the neuro-cranium. The capsular part—occipital, parietal, frontal and temporal bones—on the other hand, respond easily to the expansion of

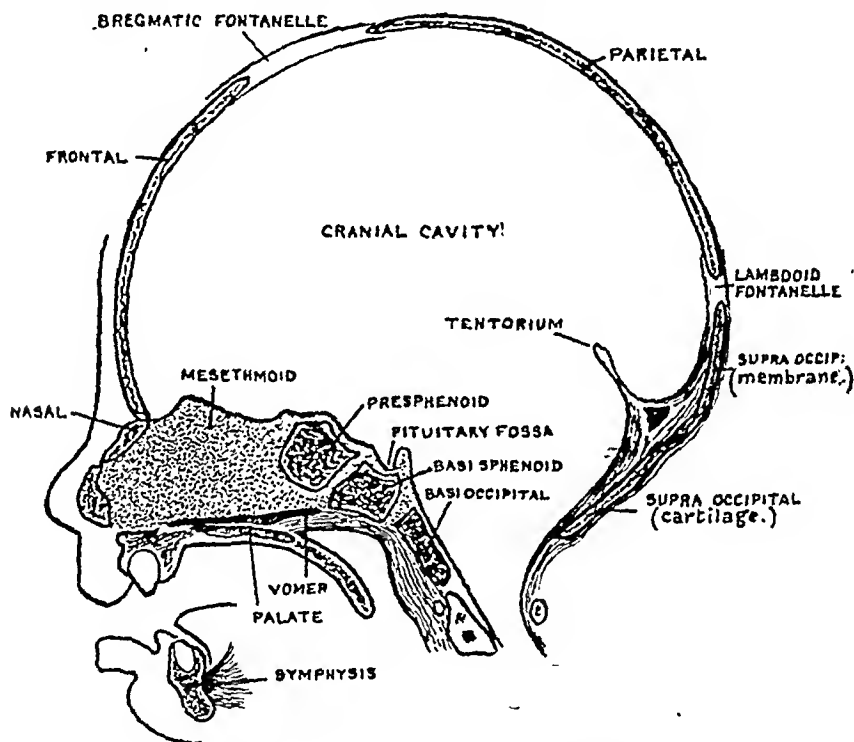


FIG. 164. Median sagittal section of the Skull of a Foetus of the 9th month.

the brain. They grow at their edges; the sutures are growth lines. Growth at the coronal and lambdoid sutures adds to the calvarial length; growth at the sagittal and squamous sutures increases the calvarial breadth. At the same time there is also a constant deposition or growth on the outer table and an absorption on the inner. In this manner the bones are modelled and remodelled, and the growth of cranial cavity and brain are co-ordinated [5]. Only those bones which enter into the formation of the cranial cavity and help to form the brain chamber are dealt with in this chapter. These bones are the frontal, parietal, occipital, temporal, ethmoid and sphenoid.

The Primitive Membranous Skull.—The brain is developed from the medullary plates of the neural groove in the same manner as the spinal

cord. As in the case of the cord the mesoderm grows under and over the cephalic part of the neural canal, and forms for it a *mesenchymal* or membranous covering. The covering of mesoderm thus formed is the primitive *Anlage* or foundation of the skull and of the brain membranes in the embryo.

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points are placed closely and soon fuse together ; (iii) for the squamosal, at the base of the zygoma (Fig. 165) ; (iv) for the membranous part of

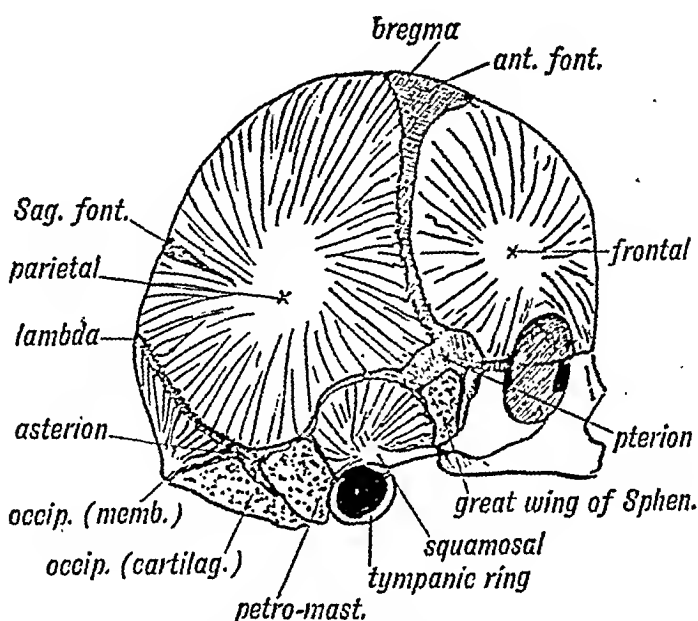


FIG. 165. The Centres of Ossification for the Dermal Bones of the Skull. The bones which are formed in cartilage are stippled.

the supra-occipital (part above superior curved line). There may be four centres (two on each side) in the membranous supra-occipital (Fig. 167).

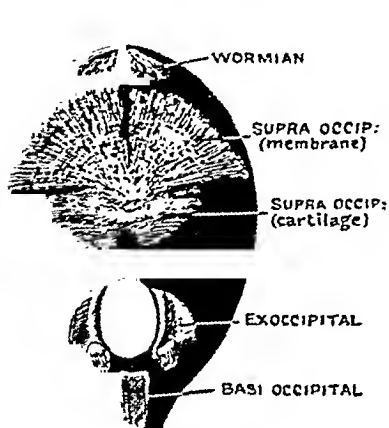


FIG. 166.

FIG. 166. The Occipital Bone at the 4th month, showing pre-interparietal Wormian bones. (After Sappey.)

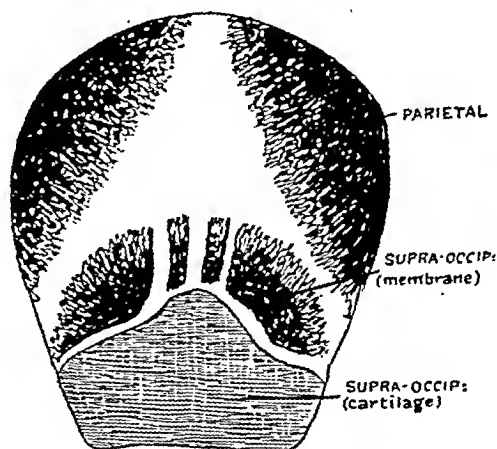


FIG. 167.

FIG. 167. The Supra-occipital from a Foetus of 3 months, showing four centres of ossification for the membranous supra-occipital. (After Maggi.)

The two or four occipital centres fuse early into one at the position of the external occipital protuberance, but occasionally these centres may form two, three or four separate bones [7]. The two frontal ossifications

fuse about the end of the 1st year or early in the 2nd; the *metopic* suture which separates them disappearing then. This suture persists in 3 to 8% of individuals according to race [8]. One or both parietals may be divided by a suture or by a complex of sutures [9]. The centres of ossification in these cases have not fused. The parietal bones begin to ossify together, at the sagittal suture, about the 22nd year, and union is usually complete by the 30th—but in many people complete obliteration may not occur until late in life [10]. The coronal suture begins to disappear a little later than the sagittal, while the lambdoid is still later and rarely disappears in its entirety. Men and women of the same age differ greatly in degree of sutural obliteration. The squamosal partly covers the petro-mastoid cartilaginous element and fuses with it in the

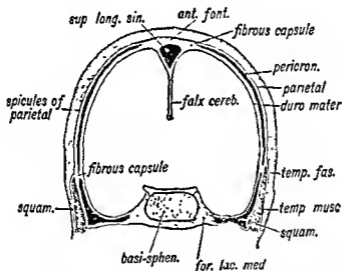


FIG 168. A coronal section of the Skull of a Foetus, 5 months old

first year, the temporal bone being thus formed. These bones, as they are laid down, accurately follow the contour of the brain. That organ forms a relatively small sphere when ossification commences. Hence the convexities or *eminences* at the regions of earliest formation.

The Manner in which these Bones are developed.—In Fig. 168 a vertical section of the skull of a foetus 5 months old is represented. The coverings of the brain are seen to be then (i) scalp, (ii) a stout white fibrous capsule, (iii) a fine membrane lining it—the inner layer of the dura mater, (iv) the arachnoid covering the brain (not shown in figure). Ossifying fibres which form the parietal are seen developing within the capsule and radiating out from the centre of ossification. The ossific fibres, as they spread outwards from a common centre, unite by cross branches, thus forming an irregular network with osteoblasts and growing vessels within its meshes. Lower down are seen the ossifying fibres

points are placed closely and soon fuse together ; (iii) for the squamosal, at the base of the zygoma (Fig. 165) ; (iv) for the membranous part of

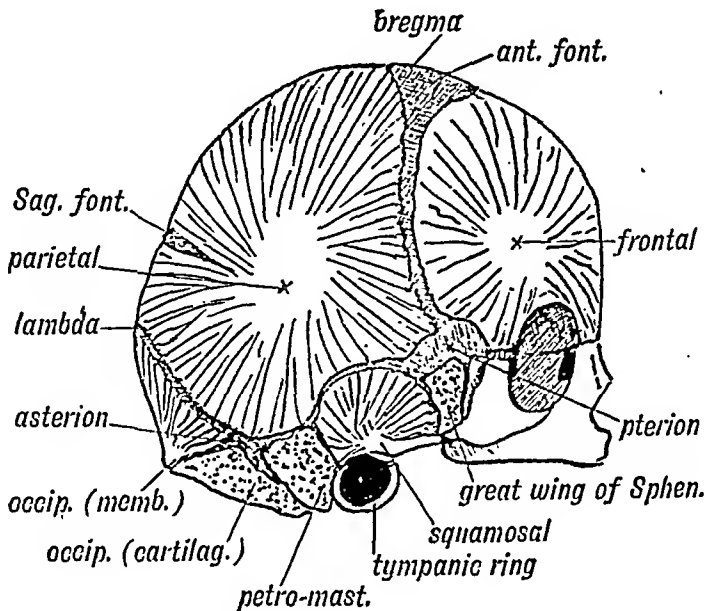


FIG. 165. The Centres of Ossification for the Dermal Bones of the Skull. The bones which are formed in cartilage are stippled.

the supra-occipital (part above superior curved line). There may be four centres (two on each side) in the membranous supra-occipital (Fig. 167).

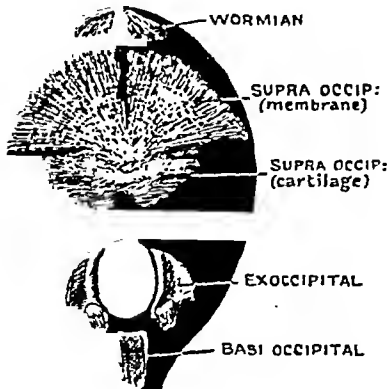


FIG. 166.

FIG. 166. The Occipital Bone at the 4th month, showing pre-interparietal Wormian bones. (After Sappey.)

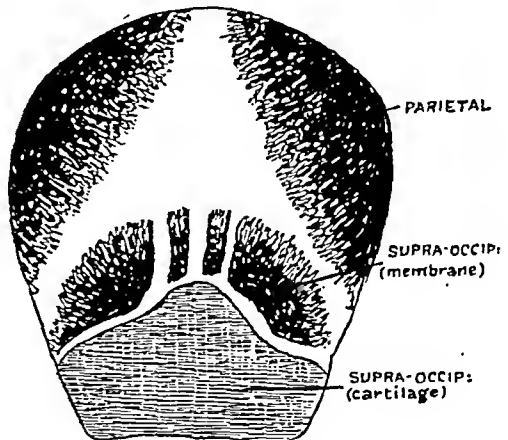


FIG. 167.

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of fibrous bone (*a, b, c, d, e*) are being extended. By the 9th year the growth tissue is exhausted and only the septum separates the edges of the two parietal bones. It is not until the septum is absorbed that union can occur, so obliterating the suture. The inner lamellae of bone are being both formed and absorbed; new ossifying fibres appear under the pericranium [13].

In Fig. 169, *B*, is shown a section of part of the parietal of the same child, made some distance from the sutural line. It will be seen that some of the trabeculae have become united, thus enclosing marrow spaces. In the 2nd year, lamellae are being laid down uniformly under the pericranium and under the dura mater, forming the outer and inner

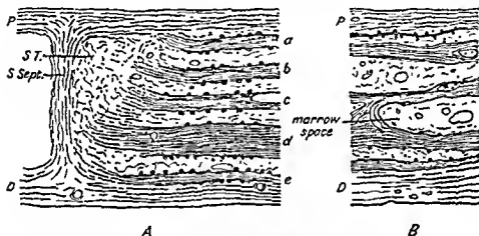


FIG 169.

A. Section across the Sagittal Suture of a Child aged 6 months. (After Bernstein)
Explanation in text.

B. Section of the Parietal Bone of the same Child made near the centre of the bone (Bernstein)

tables. It is not until the 5th year that tables and diploe become sufficiently differentiated to be clearly seen in a radiogram. Prof. H. A. Harris observed that venous spaces appear in the diploe about the age of 25, and that some 20 years later these venous spaces become filled by bone [14]. From birth to death the cranial osteoblasts are in a state of activity, laying down new bone at certain sites while at others the process of absorption goes on. The cranial bones are remodelled many times [15]. Osteoblastic activity is sensitized by hormones formed in the pituitary and in the parathyroids [16]. Even if both parietals are excised from the skull of a young animal, both are reproduced from the dural bed and assume their normal shape and contacts [17].

As the brain expands new bone is formed at the sutures to increase the capacity of the skull, but the operation of craniotomy to allow the expansion of a confined brain, by the formation of a new suture, is

of the squamosal. Between the ossifying fibres at the growing margin of the tabular bones, are parallel leashes of vessels; hence if an injection is made of the arteries, the circumference of a bone becomes intensely injected and coloured. The base of the skull is formed of cartilage which is covered, or ensheathed, by a perichondrium continuous with the membranous capsule. In the cartilage appear the centres of ossification for the sphenoid.

As the bony fibres of the parietal spread out, they divide the primitive cranial capsule into an outer layer—the *pericranium*—and an inner—the *periosteal* layer of the dura mater. At the periphery of the bone and in the sutures the continuity of these two layers persists. The growth of the fibroblasts and osteoblasts in the sutural lines between the bones keeps time with the growing brain, which expands the capsule, but there is, at each corner of the parietal bone, until the end of the 1st year, a part of the primitive cranial capsule left unossified. These unossified parts of the membranous capsule are the *fontanelles*.

The Fontanelles [11].—There are five fontanelles connected with each parietal bone, one at each of its rounded angles, and one, the *sagittal* (Fig. 165), which occurs between the radiating fibres of the parietal near the posterior end of the sagittal suture. The parietal foramen marks its position in the adult. In about 30% of children this fontanelle is unclosed at birth (Adair and Scammon); a large *parietal foramen* may permanently mark its situation [12]. The posterior inferior fontanelle, situated at the *asterion* (Fig. 165), the anterior inferior, at the *pterion*, and the posterior superior, at the *lambda*, close before or about the time of birth. Separate or detached ossifications, which become *Wormian* bones, are often developed in the primitive capsule of the skull at those three fontanelles and thus close them. The anterior superior fontanelle, at the *bregma*, cannot be distinctly felt during life after the 1st year (Warner), but it is not completely closed until the 2nd year is nearly over. This fontanelle is lozenge-shaped, being bounded by four bones, viz. the two parietals and two frontals. The bregmatic or anterior superior and lambdoid or posterior superior fontanelles are median and common to both parietals.

Differentiation of Tables and Diploe.—In Fig. 169 is given a diagrammatic section across the sagittal suture of a child aged 6 months. The tissue occupying such a suture has been compared to a growth or diaphysial disc of a long bone. There is, however, one important difference. It will be seen that, in the midst of the suture, the pericranium (*P*) and dura mater (*D*) are united by a septum of tissue, which we may speak of as the sutural septum (*S. Sept.*). On each side of this septum is situated the growing sutural tissue (*S.T.*), into which spicules

vertebrae, the lateral processes, corresponding to the neural vertebral arches and an extra element—the tectal plate.

In Fig. 171 the condition of the occipital region is shown in a 5th-

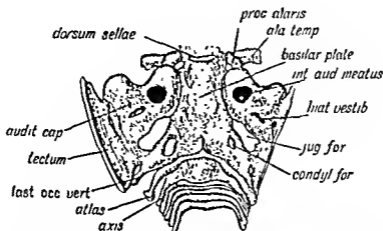


FIG. 170. Intracranial aspect of the Basal Plate and Occipital Parts of the Chondrocranium of a Human Foetus in the 8th week of development (Warren Lewis)

month foetus. Four centres of ossification appear in the tectum (Fig. 167), and quickly fuse to form the membranous part of the supra-occipital. A suture between the membranous and cartilaginous parts

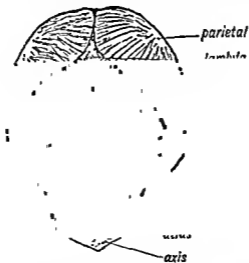


FIG. 171. The Occipital Region in a Foetus of 5 months.

is clearly visible—especially near the fontanelle at the asterion. The membranous and cartilaginous parts of the supra-occipital become completely fused soon after birth. It will be observed that the process of fusion between the lateral parts of the cartilaginous supra-occipital is not complete in the 5th month (Fig. 171). The occipital fontanelle

founded on the assumption that the arrest of brain-growth in microcephalic idiots is due to the closure of the sutures, whereas it is due to an inherent defect in the brain. We frequently see skulls where one or more sutures have been prematurely closed, but in such cases there has been compensatory growth at other sutures, giving rise to a peculiarity in cranial form. Growth of the cranial cavity could take place by a deposit of bone on the outer table and an absorption from the inner: for this manner of growth, sutures are unnecessary. The synostosis of the sutures does not necessarily prevent growth; synostosis of the skull bones occurs only when the brain has ceased to expand. If the brain of the infant is arrested in its growth, premature ossification of the sutures occurs, the condition of *microcephaly* resulting therefrom [18]. In *hydrocephaly*, when the ventricles become enormously dilated, the membranous capsule of the cranium expands so quickly that the process of ossification cannot keep up with its rapid growth. Hence in hydrocephaly the fontanelles are enormous. The growing points of ossific fibres become detached and form Wormian bones. The cartilaginous part of the skull is scarcely affected in this disease. The membrane-formed part of the skull is liable to diseases which do not affect the cartilage-formed part. The dura mater is very adherent to the bones formed in cartilage.

Development of Bones formed in Cartilage.—(i) *The Occipital Bone.*—The occipital bone is developed from the *parachordal cartilages*. Two cartilaginous bars, although appearing separately in the development of fishes, are united from their first appearance in the human embryo, forming a *basilar plate* (Robinson). The plate is formed in the mesenchymal sheath of the notochord, its centre of chondrification—the first to appear in the base of the skull—beginning at the end of the 1st month of development. The basilar plate may be regarded as a continuation of the vertebral bodies, while the lateral processes (Fig. 170), which are perforated at their bases by the foramen or foramina for the hypoglossal nerve and which separate the jugular foramen in front from the foramen magnum behind, may be regarded as a continuation of the neural arch series [19]. Fused to the lateral process and also to the otic capsule is the roof plate already mentioned—the tectal plate or tectum (Fig. 170). While the lateral processes never reach the posterior or dorsal margin of the foramen magnum, it is quite otherwise with the right and left tectal plates; they extend round the hind-brain until they meet and unite, thus forming the posterior margin of the foramen magnum and the supra-occipital plate of cartilage. Thus the cartilaginous basis of the occipital bone is formed out of three elements on each side—the basilar plate representing the centra and hypochordal arches of cervical

vertebrae, the lateral processes, corresponding to the neural vertebral arches and an extra element—the tectal plate.

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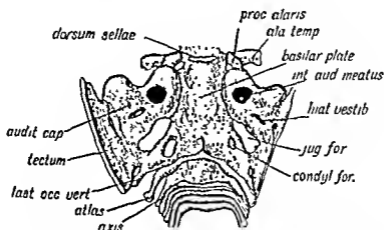


FIG. 170. Intracranial aspect of the Basal Plate and Occipital Parts of the Chondrocranium of a Human Foetus in the 8th week of development. (Warren Lewis)

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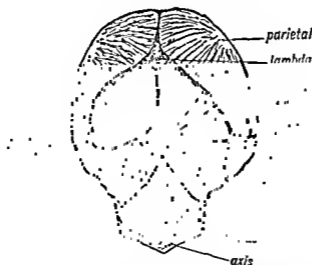


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The hinder ends of the trabeculae fuse with the parachordal cartilages round the anterior termination of the notochord. The stalk of the pituitary becomes enclosed in the intertrabecular plate. In front of the pituitary the two trabeculae are fused in the middle line. The mesial fused parts of the trabeculae become the embryological basis of the nasal septum (Fig. 173). The posterior part of the median fused bars forms the cartilaginous basis of the pre-sphenoid and basi-sphenoid [21]. The trabeculae, as we shall see later (p. 230), have a very ancient lineage. They belong to the same series of structures as the cartilages of the

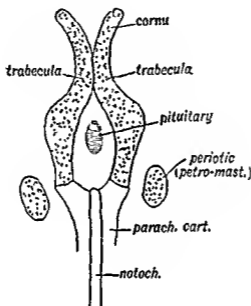


FIG. 172 Diagram of the Trabeculae Cranii, Parachordal Cartilages, and Periotic Capsules

gills. The trabeculae represent the cartilaginous arch of the pre-mandibular or first segment of the head.

Development of the Sphenoid.—Prof. Fawcett observed the manner in which the cartilaginous basis of the sphenoid is formed in the human embryo [1]. The mesodermal or mesenchymatous basis of the sphenoid becomes chondrified during the 2nd month—right and left centres representing the original trabeculae. While the cartilage, in which the centres for ossification of the basi- and pre-sphenoids appear, is formed out of the trabecular or prechordal plate, the great and small wings have separate origins. We have already seen (p. 207) that on each side of the prechordal base there are formed two plates of cartilage, rudiments of the lateral wall and roof of the primitive cartilaginous cranium (Fig. 162). The anterior of these—the *orbito-sphenoids*—form the cartilaginous basis of the lesser wings. In the 8th week of development (Fig. 173) each is a

projects upwards between them from the foramen magnum. This fontanelle is filled by a continuation of the posterior atlanto-occipital ligament, and becomes closed soon after birth. It is the most common site of a cerebral meningocele—a saccular protrusion of the membranes of the brain which contains cerebro-spinal fluid, and usually a part of the occipital lobes distended by a dilatation of the posterior horns of the lateral ventricles.

Separate centres of ossification appear early in the 3rd month of foetal life in the occipital cartilages to form (i) the basi-occipital, (ii) the two exoccipitals, and (iii) the supraoccipital [20]. The occipital consists of four pieces until the 4th year, when synostosis occurs. The occipital condyles are formed from the exoccipitals and basi-occipital, the exoccipital element constituting in the adult by far the larger part, but when the condyles first appear they are continuous at the anterior border of the foramen magnum, forming a single or median condyle, as in reptiles, birds and lower mammals. The foramen for the hypoglossal nerve, which may be subdivided into two or even three compartments, is formed between the two elements and thus corresponds to the inter-vertebral series. The occipital protuberance at the inion is formed by both membranous and cartilaginous parts of the supra-occipital. One or two Wormian bones are often formed in the occipital fontanelle at the posterior border of the foramen magnum and receive the fantastic name of the bones of Kerckring.

(ii) *The Petro-mastoid* forms part of the base of the skull. We shall see that the petrous bone (p. 323) is primarily developed as an independent cartilaginous capsule round the inner ear, but at an early date (6th week) it fuses at certain points with the parachordal basis of the occipital bone, while an extension from the mastoid part of the capsule enters into the formation of the tectum. Even as late as the 30th year remnants of the tectal cartilage may be found between the petro-mastoid and occipital bones, especially between the jugular process of the occipital and the mastoid. The fibro-cartilage in the foramen lacerum medium and perhaps the Eustachian cartilage, which is continuous with it, are remnants of the periotic cartilaginous capsule.

(iii) *Trabeculae Cranii*.—The basilar plate, containing the notochord and fashioned out of the parachordal cartilages, terminates immediately behind the pituitary fossa. The cartilage of the dorsum sellae is a separate formation. The prechordal part of the base of the skull in the lowest vertebrates appears first as two irregular plates of cartilage—the trabeculae cranii (Fig. 172). Even in the mammalian skull the trabeculae can still be traced in the pituitary region, where they are united by a plate of cartilage, ultimately included in the floor of the pituitary fossa.

from the palato-quadrate bar. Thus many structures on the intra-cranial surface of the body of the sphenoid and on the great wing are, in a morphological sense, extra-cranial, namely, the cavernous sinus, the internal carotid artery, the IIrd, IVth and VIth cranial nerves.

At birth the sphenoid bone consists of three parts, the great wings being separated from the rest of the bone. The *sphenoidal turbinate* bones, afterwards inflated by the development of the sphenoidal air sinuses, are then nodules of bone surrounded by cartilage. They also

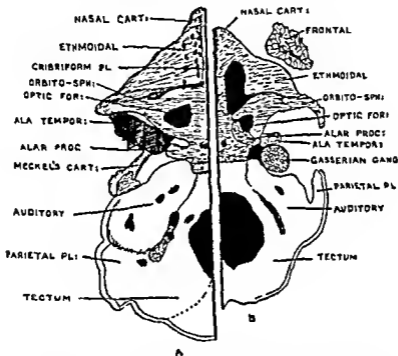


FIG. 174.

A. Left half of the Cartilaginous Basis of the Skull in a foetus of 3½ months.
(After Kollmann.)

B. Right half of the Cartilaginous Basis of the Skull in a foetus of 2½ months.
(After Fawcett.)

are separate and are derived from the lateral ethmoidal cartilaginous plates, which represent the olfactory capsule [23]. The *internal pterygoid* plates are also separate ossifications laid down in the membrane covering a plate of cartilage. This cartilage represents part of the palato-quadrate bar of lower vertebrates (Fig. 163). Only its hamular process is formed in cartilage (Fawcett). The internal becomes adherent to the external plate during the 4th month of foetal life. The external plate is developed as a membranous outgrowth from the alisphenoids, or great wings. The pre-sphenoid unites with the basi-sphenoid in the 8th month; the great wings unite with the basi-sphenoid soon after birth. The *lingula* (alar

sickle-shaped plate lying over the stalk of the optic vesicle, sending one process under the optic nerve to join the cartilaginous prominence—the *processus hypochiasmatica*—from which the muscles of the eyeball take origin. The other process of the orbito-sphenoid fuses with its fellow above the prechordal plate and thus completes the optic foramina (Fig. 174). The great wing or *alisphenoid* arises in a rather complicated manner. In the 8th week it is represented by two small nodular masses of cartilage (Fig. 173), the alar process attached to the prechordal plate and the temporal wing. The internal carotid artery lies on the mesial side of the alar process, which is represented by merely the lingular process in the fully developed bone. The temporal wing lies under the

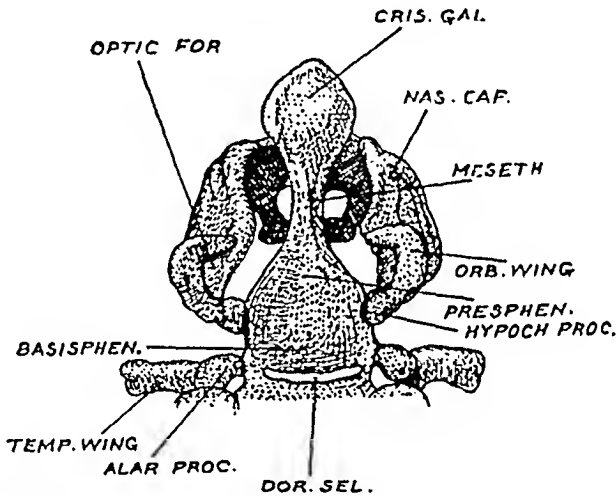


FIG. 173. The Prechordal Base of the Chondrocranium in the 8th week of development. (Warren Lewis.)

Gasserian ganglion and separates the 2nd from the 3rd division of the nerve [22]. The mesodermal tissues round the temporal wing undergo a secondary chondrification, and it is from this new formation that the greater part of the alisphenoid is formed; as it extends it encloses the 2nd and 3rd divisions of the Vth nerve, the round and oval foramina being thus formed (Fig. 175). A gap remains between the orbito-sphenoid and alisphenoid to form the sphenoidal fissure. The dorsum sellae has a separate centre of chondrification.

The small size of the alisphenoid in its first stage of development and its remarkable growth in its later stages may be explained by its evolutionary history. It has been evolved from an element which did not originally enter into the formation of the cartilaginous cranium—the *palato-quadrate*. With the evolution of a temporal lobe there necessarily appeared a middle fossa in the base of the cranium to contain it. The element which expanded to form a wall for the middle fossa was derived

(i) By the union of two bones : examples of this form are the jugular foramen, sphenoidal fissure, Glasserian fissure, etc.

(ii) By the union of two elements of one bone : the anterior condylar foramina, optic foramina, the foramen magnum, aqueductus Fallopii, etc.

(iii) By the enclosure of a notch on the edge of a bone, of which the foramen ovale is the best example. This foramen is at first a notch in the posterior border of the great wing of the sphenoid (Fig. 175) ; it remains in this condition in all mammals except man and some anthropoids. In man the margins of the bone on each side grow out and fuse, and thus convert the notch into a foramen. Other examples are the foramen spinosum, the foramen rotundum, parietal foramen, mastoid,

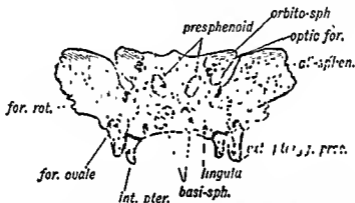


FIG. 175. The Sphenoid in a foetus of 4 months. The centres of ossification are deeply shaded. (After Sappey.)

and the internal auditory meatus, which appears first as a notch on the upper border of the petrous cartilage.

Wormian Bones.—In the six fontanelles which occur at the parietal angles ossific centres frequently appear. Fontanelle ossifications form Wormian bones. They occur most frequently at the posterior angles of the parietal (Lambda and Asterion) ; they are also common at the Pterion (epipteric Wormian), but rare at the Bregma. The Wormian at the last-mentioned point receives the name of *os anti-epilepticum* ; another may form in the occipital fontanelle—the *os kerckringi*. Much confusion has been caused by naming a large Wormian which may occur in the lambdoidal (posterior-superior) fontanelle the inter-parietal bone. Wormian or sutural bones are particularly numerous in the skulls of infants who have been the subjects of hydrocephaly. It is possible that, during the rapid expansion of the skull, the tips of ossifying fibres become detached, thus forming separate centres of ossification in the sutures and fontanelles.

Inter-parietal Bone.—It has already been shown that the part of the

proc., Fig. 174, *B*) which bounds the outer side of carotid groove is ossified from a centre which appears during the 4th month of foetal life.

The wings of the sphenoid developed in the orbital region of the primitive skull (Fig. 163). The enormous expansion of the cerebral vesicles and the evolution of a new mode of mastication have worked a revolution in the primitive orbital region; the temporal lobes, as it were, have burst the ancient cartilaginous wall. The ala-temporalis appears first in the embryo as a process from which the muscles of mastication take origin (Fawcett).

The pituitary body is developed between the trabeculae cranii; the pre-sphenoid is formed in front of it and the basi-sphenoid behind it. A canal may remain in the foetal or even adult bone to mark the position of the developmental stalk of the buccal part of the pituitary [24]. On the cerebral aspect this canal opens at the olivary eminence which also marks the union of the pre- and the basi-sphenoids. The writer has seen a child in whom the trabecular cartilages had remained apart, leaving a wide gap through which the pituitary projected within the septum of the nose. The pre-sphenoid and afterwards the basi-sphenoid are much altered by the growth of the sphenoidal sinuses, which commence to expand rapidly about the 7th year [25]. The great wings support the temporal poles of the brain, their size depending on the development of that part of the brain. They are much larger in man than in any other mammal, owing to the great size of the human temporal lobes. The small wings project within the vallecule Sylvii. In the early foetus the dorsum sellae is enormously developed, and fills the deep and sharp angle between the mid-brain and fore-brain (Fig. 107).

The Ethmoid.—The cartilaginous basis of the skull is completed in front by the ethmoid; on its upper surface rest the olfactory bulbs. In the primitive skull (Figs. 160, 163) the olfactory capsule, out of which the cartilaginous ethmoid has been evolved, is far in front of the space which contains the fore-brain. In the evolution of the higher vertebrates the frontal lobes have been brought within the floor of the cranial cavity by a double process—by a shortening of that part of the trabecular plate which unites the sphenoid to the olfactory or ethmoidal capsule, and by the forward extension of the cerebral vesicles, which have pushed their way into the forehead until they project beyond the olfactory region. The cribriform plate is formed in the 4th month; until then a gap separates the lateral mass from the septal or trabecular plate (Fig. 174, *A*, *B*).

Formation of Foramina in Bone.—The foramina of the skull are formed in one of three ways (Bland-Sutton):

occipital poles of the brain; the breadth or widest diameter is measured between the widest points—usually some distance below the parietal eminences. If the length of a skull is 100 mm. and the breadth 75, the cephalic index of that skull is 75, *i.e.* the breadth is 75% of the length. Human races may be *dolichocephalic* (long-headed), the breadth being 75% or less of the length; *brachycephalic*, in which the breadth is 80% or more of length; or *mesaticephalic*, in which the breadth is between 75% and 80% of the length. Various methods are employed in estimating the height of the skull, but the best is that which takes the upper margin of the external auditory meatus and lower margin of the orbits as representing the basal (Frankfort) plane. The height is measured from this plane to the highest point in the sagittal suture [26]. The vault attains its greatest height above the external meatus about the 8th year. After then, the basal parts widen and lengthen, while the height of the vault remains about the same level. After the 8th year a child's skull changes greatly in its contours.

English people have an average cephalic index of 78, South Germans 83; but it must be remembered the individuals of every race show a wide range of variation [27]. It will be seen that the topography of the brain worked out by German surgeons cannot be applied to the longer English heads without modification.

Factors which determine the Shape of Head.—The shape of the skull depends: (i) on the size and shape of the brain; (ii) on the size and strength of the muscles which arise from it—the muscles of mastication; or are inserted to it—the muscles of the neck. Brain growth is by far the most important factor, but we do not know the conditions which flatten the brain from side to side in dolichocephalic races or shorten it from frontal pole to occipital pole in brachycephalic races. Muscular action can only exercise a minor effect. Prof. Arthur Thomson [28] has shown that there is a relationship between dolichocephaly and the size of the temporal muscles—which are relatively large in long-headed races—and the shape and mechanism of the mandible. It is to be remembered that: (i) the muscles of mastication and of the neck undergo their greatest development between the 12th and 28th years; (ii) before that time the brain has almost completely attained its adult size and shape; (iii) with the growth of the face and neck, at and after puberty, the basal parts of the skull and brain are widened, but the ratio of cranial width to length—save for the growth forwards of frontal sinuses and glabella—remains nearly the same. On the other hand, the ratio of width to length may alter greatly between birth and childhood [29].

It has been inferred that the shape of the skull and head depends on

supra-occipital above the superior curved lines is developed from membrane by four centres of ossification, and is at first, and remains so almost until birth, nearly separated from the lower part developed from cartilage (Figs. 167, 171). The membranous part of the supra-occipital represents the inter-parietal bone. In marsupials, ruminants and ungulates the inter-parietals fuse with the parietals, and not with the occipital. In rodents they fuse with both occipitals and parietals. In primates and carnivora, as in man, they fuse with the occipital. It is extremely rare to find the whole inter-parietal as a separate bone in man, but a large Wormian, partly replacing the inter-parietal, is very

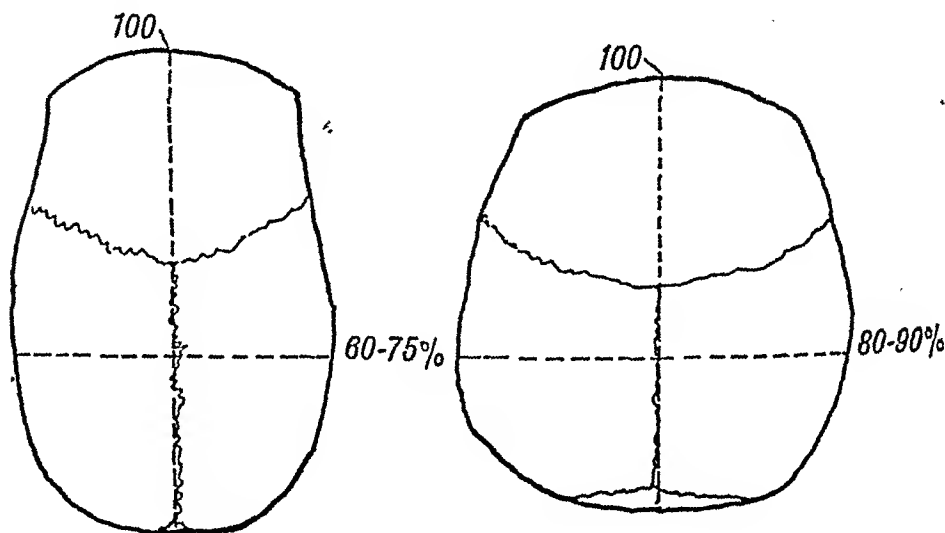


FIG. 176.

A. Diagram of a Long-head (Dolichocephalic).

B. Diagram of a Short-head (Brachycephalic).

frequent. Such a Wormian bone, if large, is named variously *os epactal*, *os Incae*, *os triquetrum*, or *pre-interparietal*.

The *Post-frontal* does not occur in mammals as a separate bone; in them it has fused with the frontal, and forms that part of the bone which articulates with the great wing of the sphenoid and malar. A Wormian bone—the *epipteric*—which is occasionally developed in the fontanelle at the pterion may be mistaken for it. Traces of a true post-frontal, partly separated from the frontal, rarely occur in man.

The Cephalic Index.—Anthropologists have employed the shape of the head as a character in classifying the races of mankind. The *cephalic index* is used to express the shape of the head. It states the proportion that the breadth bears to the length of the skull (Figs. 176, A, B). The length or *long diameter* of the skull is usually measured from the glabella to the most projecting point of the occiput—commonly situated over the

are shown. They are contrasted types; in one, *Acrocephaly* or steepleskull, the base is abnormally short, owing apparently to an arrest of growth at the junction of the pre-sphenoid and ethmoid. Compensation is obtained by an upward growth of the brain, thus heightening the roof. In severe cases the optic nerves may be pressed on and blindness thus caused. In the second type, *Scaphocephaly*, or boat-shaped skull, the cranium is very narrow from side to side, while the calvarial arc—from nasion to opisthion (posterior border of foramen magnum)—is greatly elongated. In scaphocephaly there is an arrest of growth—often a synostosis—along the sagittal suture. In *acrocephaly* the coronal suture is closed. In these two and in allied conditions there is a certain

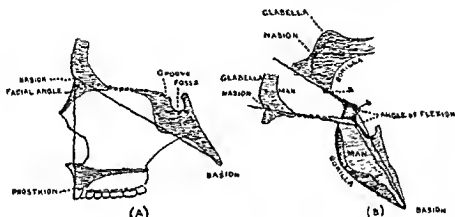


FIG. 178.

A The Facial Angle as determined by the line from the Nasion to the Prosthion.

B The Facial Angle as determined by the line from the Nasion to the Basion.

Amount of the angle increasing at B.

amount of evidence that points to a disturbance in the function of the glands of internal secretion.

The *Facial Angle* is the angle at which the face projects from the axis of the skull (Figs. 178, 179). The skull consists in man, as in all mammals, of two parts—the facial part (splanchnocranium), which carries the teeth and is developed according to their size, and the *brain capsule* (neurocranium), which depends on the size of the brain. The smaller the brain and the larger the face, the more does the face project in front of the skull, and, therefore, the greater is the facial angle, and *vice versa* [33]. It will thus be seen that the facial angle is to a certain degree an index of brain development, although it is greatly influenced by the state of the jaws. It is smallest in the most highly developed races of man; it is larger in the lower races, and larger still in the anthropoids; it increases in size with the advent of the permanent teeth

the rate of growth at the sutural junctions, growth being greatest at the coronal and lambdoid sutures in long heads, and at the sagittal and squamosal in wide heads. Investigations have proved that sutural additions have a minor influence on head-form. Premature obliteration of a suture, or of part of a suture, may produce no apparent alteration in cranial shape [30].

Abnormal Crania [31].—It is possible that light will be thrown on the factors which determine head-form by the study of certain pathological conditions. In the disease known as acromegaly, where there is always

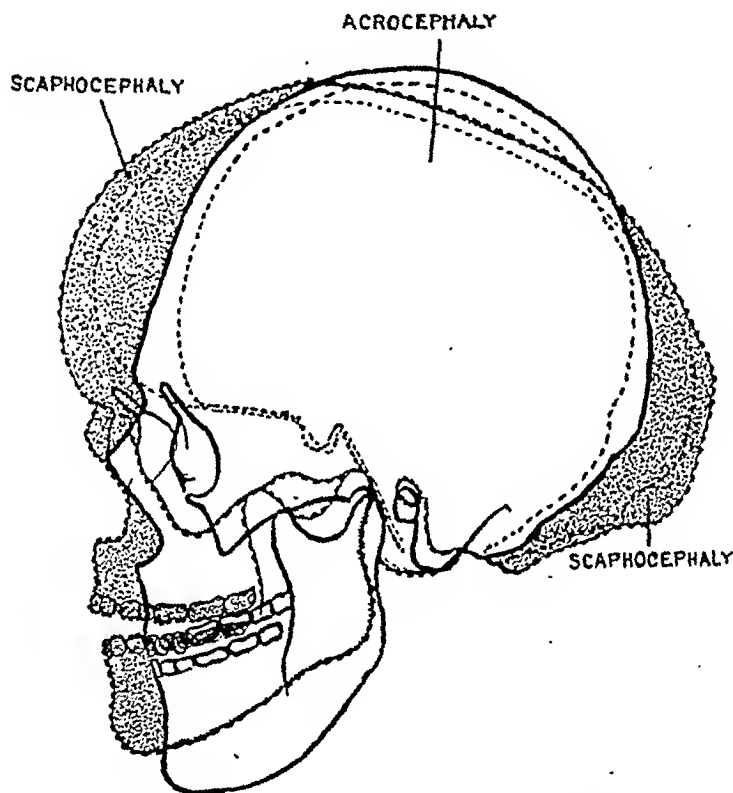


FIG. 177. Outlines of Abnormal Skulls, showing a contrast in shape.

a great enlargement of the pituitary gland, the skull undergoes peculiar growth changes. The supra-orbital ridges become greatly developed the face elongates, the temporal lines from which the temporal muscles arise, grow upwards on the side of the skull, thus increasing the area of the temporal muscles. At the same time the lines which mark the attachment of the muscles of the neck—the mastoid processes, superior curved lines and external occipital protuberance—also increase greatly in size. In achondroplasia and in rickets the skull assumes characteristic forms due to a disturbance in the growth of the base of the skull. To a certain degree the growth of the cranial bones is regulated by internal secretions [32]. In Fig. 177 two common types of abnormal skull forms

The *para-mastoid* process projects from the temporal bone lateral to the para-occipital (Parsons). If we regard the jugular process of the occipital as representative of a transverse process, then the para-occipital process may be of the same nature as the bony union occasionally seen between adjacent transverse processes of cervical vertebrae.

Ungrowth of the Temporal and Occipital Ridges or Curved Lines.—In lower animals, such as the ape or dog, a great increase in the development of the temporal and nuchal muscles takes place with the eruption of the permanent teeth, the area of their origin from the skull being necessarily enlarged. The ridges of bone which mark the limit of attachment of these muscles, the temporal and occipital ridges, ascend on the skull as waves of living bone before the growing muscles. The ridges may meet, as in apes, along the sagittal and lambdoidal sutures and form great crest-like upgrowths. In Fig. 179 the position of the temporal lines in a juvenile chimpanzee is shown; they are approaching the sagittal suture. They have extended backwards, and met with the occipital lines, which are ascending above the attachment of the growing muscles of the neck. The temporal and occipital lines are seen to be fused together to form a temporo-occipital crest. At the same time the temporal lines spread forwards on the frontal region, the frontal extension being accompanied by a marked growth of the supra-orbital ridges and of the zygomatic arches. Thus the skull is modified by the growth of the muscles of mastication and of the neck. In man these changes also take place, but to a less extent than in anthropoids. At birth the temporal lines are just above the lower border of the parietal bones. During the second year the mastoid part of the ridge for the attachment of the neck muscles grows downwards into a pyramidal process—the mastoid—which is peculiar to the human species. In Neanderthal man the mastoid process is shaped as in the anthropoid infant [34].

Segmentation Theory of the Skull [2].—It is inferred from investigations made on the developing heads of fishes and amphibians that each primitive cephalic segment contains a cavity comparable to that seen in each body segment (p. 59), from the wall of which are developed (see Fig. 180): (i) a sclerotome, (ii) muscle plate, (iii) skin plate, (iv) modified nephrotome. The sclerotome of each segment provides a cartilaginous sheath for the notochord and the basis of the cranial capsule. The three hinder segments (occipital) give rise to muscle plates (Fig. 180). The ventral or visceral part of each segment, as is shown in Fig. 180, descends by the side of the foregut, to fuse together ventral to that tube, where they enclose the pericardium. Out of the ventral parts of the segments are fashioned the branchial or visceral arches. We have already noted the fact that an essential element of the branchial arches

and the necessary increase in the size of the face. It is, therefore, greater in the adult than in the newly born.

Flexion of the Cranial Base.—In Figs. 178, *A*, and 179 the axis of the cranial base is represented by a line drawn from basion to nasion, but it is quite apparent that this line does not represent the axis accurately. The truth is that there are two parts in the cranial axis which are functionally as well as morphologically distinct, the chordal and prechordal parts (p. 206). In the higher primates, especially in man, the prechordal part is bent downwards—or flexed—on the chordal. The manner in which the degree or angle of flexion may be measured is shown

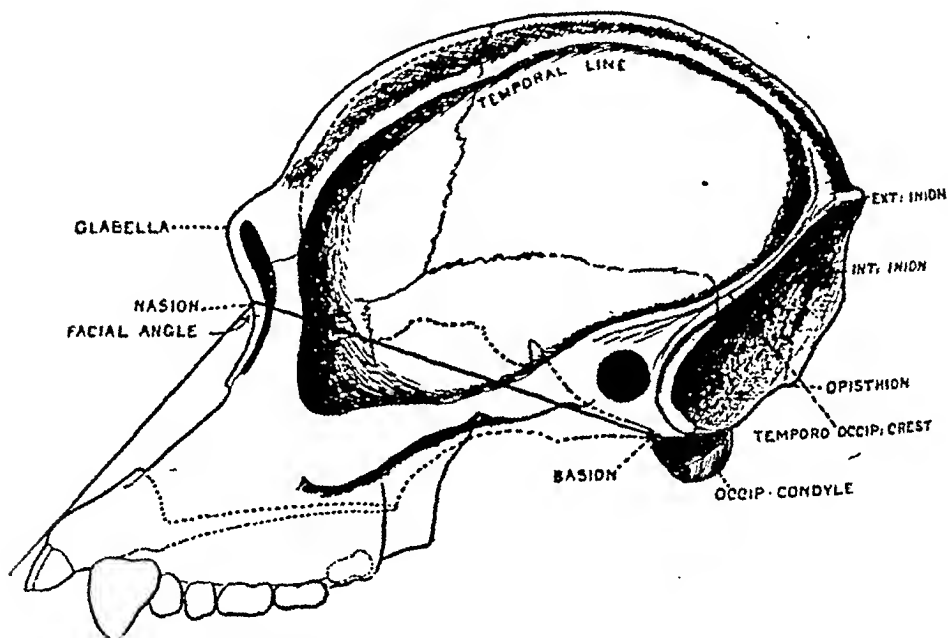


FIG. 179. Profile of the Cranium of an Immature Chimpanzee, showing the ascent of the temporal ridges, the formation of occipital crests and the lines of the facial angle.

in Fig. 178, *B*; it is a much opener angle in anthropoids than in man. The degree of flexion is most variable in man; in cases where the flexion is great the forehead is projecting and the face receding, the facial angle being apparently small. If there is a great degree of extension of the axis, then the forehead is receding and the lower part of the face projecting or prognathous. Thus the facial angle is not a safe guide to the degree of prognathism or face projection, because it may be exaggerated or masked by the extension or flexion of the cranial base.

The *Para-occipital Process* is sometimes present in man, and projects downwards from the jugular process of the occipital bone. The rectus capitis lateralis is inserted to it. The process represents the para-occipital process, which is so highly developed in rodents and ungulates.

The *para-mastoid* process projects from the temporal bone lateral to the para-occipital (Parsons). If we regard the jugular process of the occipital as representative of a transverse process, then the para-occipital process may be of the same nature as the bony union occasionally seen between adjacent transverse processes of cervical vertebrae.

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is derived from the neural crest (p. 71) and also that the mesoderm by the side of the foregut is separated at a very early phase of development.

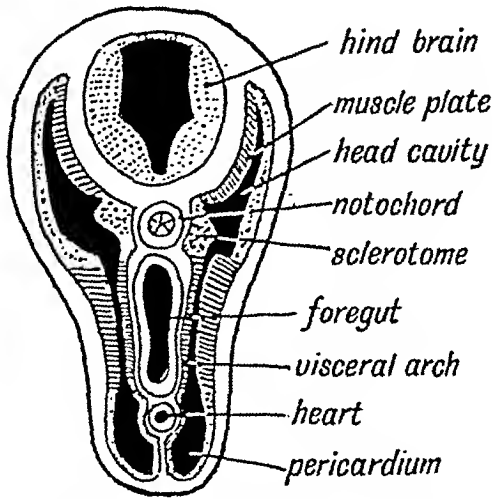


FIG. 180. Scheme of Segmental Head-cavity seen in a section made in the coronal plane.

The number of segments in the mammalian head is by no means settled; on the evidence of the cranial nerves and of the neuromeres

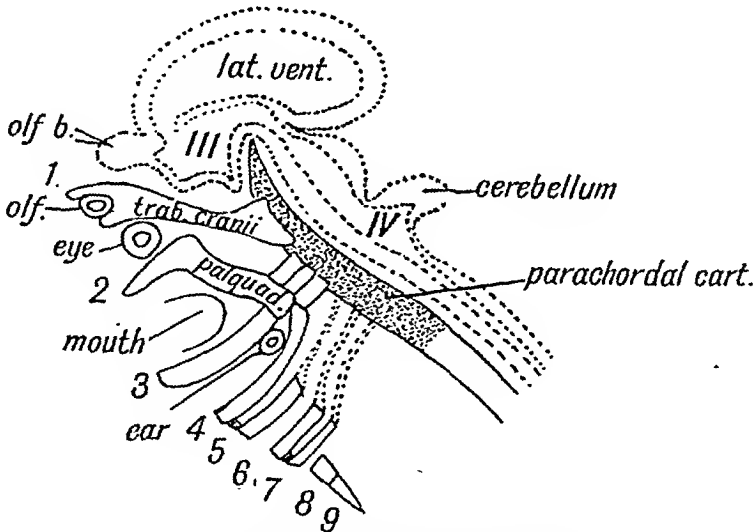


FIG. 181. A schematic diagram of the Segmental Elements of the Skull. The numbers refer to the cartilaginous bars of the various visceral arches. The 4th and 5th are combined in the hyoid bone, the 6th and 7th in the thyroid cartilage, the 8th (and 9th?) in the arytenoid, cricoid, and tracheal cartilages. For further explanation, see note [35], p. 233.

of the hind-brain the number appears to be seven (p. 151), but certain considerations, specially relating to the facial and branchial structures, which we proceed to examine in the next chapter, lead us to suspect that the number is nine.

In Fig. 181 a diagrammatic representation is given of one of the many

segmental theories of the skull. The parachordal plate represents the unseparated centra of the nine segments. The primitive neural arches have been disturbed by the enormous enlargement of the neural tube, but especially by the expansion of the tube in the prechordal region to form the cerebrum and basal ganglia. In amphioxus the neural tube does not extend beyond the notochord. In the vertebrate head all that remains of the *neural arches* of the nine primitive segments are the lateral occipital cartilaginous processes (Fig. 170). Of the visceral cartilaginous processes of the nine segments the 1st form the trabeculae cranii (Huxley, Howes); with the forward protrusion of the neural tube the trabeculae come to form part of the base of the skull; the 2nd form the palato-quadrate bars [35]. Both of these processes are preoral. The 3rd forms the mandibular bar, the 4th the hyoid bar, the 5th, 6th, 7th, 8th form the cartilaginous bars in the 1st, 2nd, 3rd and 4th branchial arches. The reader will see that if the first and last cartilage are rejected as having no segmental significance, the theory put forward here is identical with that formulated in connection with the cranial nerves. We are at least justified in assuming that the parachordal part of the skull is the oldest, and is therefore known as the *palaeocranium*; whereas the prechordal part is more recent and is for this reason known as the *neocranium* [36]. Further details relating to the facial and pharyngeal parts of the head will be given in the following chapters.

Gaskell's Theory.—Gaskell regarded the trabecular or prechordal part of the vertebrate head as a derivative of the prosoma, and the parachordal part from the mesosoma of an invertebrate form such as is now exemplified by the Kingcrab (*Limulus*). The prosoma carries 7 pairs of appendages, which surround the mouth. The last of these represents the mandible, the first, the nasal processes; the intermediate appendages are combined in the maxillary processes. The mesosoma carries processes which serve for respiration and locomotion. In vertebrates these are modified to form branchial arches [37].

NOTES AND REFERENCES

[1] For an account of the development of the human skull, see Frazer, J. E., *Manual of Embryology*, 1940; of vertebrate skull, De Beer, G. E., *The Development of the Vertebrate Skull*, 1937 (full literature); Fawcett, E., *Jour. Anat.*, 1923, 57, 299 (30-mm. and 48-mm. foetuses).

[2] For segmentation of the head, see De Lange, D., *Jour. Anat.*, 1936, 70, 515; De Beer, G. E., see preceding note; Allis, E. Phelps, *ibid.*, 1938, 72, 584; Kesteven, H. L., *ibid.*, 1933, 67, 443; Desai, P., *Archiv. Biol.*, 1932, 43, 30.

[3] For growth of foetal brain, see Jenkins, G. B., *Contrib. Emb.*, 1921, 13, 43; Herdorfer and Scammon, see note [12], Chapter XI.

[4] For closure of sutures, see Todd and Lyon, *Amer. Jour. Phys. Anthropol.*,

1924, 7, 325; *ibid.*, 1925, 8, 23, 47, 149; Ashley Montagu, M. F., *ibid.*, 1938, 23, 355; Bolk, L., *Amer. Jour. Anat.*, 1915, 17, 495 (on the premature obliteration of sutures).

[5] For remodelling of cranial bones during growth, see Brash, J. C., *Edin. Med. Jour.*, 1934, 41, 305; Todd and Tracy, *Amer. Jour. Phys. Anthropol.*, 1930, 15, 53.

[6] For ossification of cranial bones, see De Beer, G. E., preceding note [1]; Augier, M., *Traité d'Anatomie Humaine* (Poirier and Charpy), 1931; Limson, M., *Contrib. Emb.*, 1932, 23, 207 (based on 163 foetuses).

[7] For early development of the human occipital, see Augier, M., *Archiv. Anat. Hist. Emb.*, 1931, 13, 33; Lacoste, A., *ibid.*, 1931, 12, 3; see also reference to Fawcett in preceding note [1].

[8] For recent observations on metopic suture, see Weidenreich, F., *Trans. Amer. Phil. Soc.*, 1941, 31, 321; Schultz, A. H., *Contrib. Emb.*, 1937, 26, 73 (in apes); Ashley-Montagu, M. F., *Jour. Anthropol. Instit.*, 1937, 67, 157.

[9] Patten, C. J., *Zeitsch. Anthropol. Morph.*, 1912, 14, 527; see also reference to Limson, L., in preceding note [6].

[10] Todd, T. W., *White House Conference Publications*, 1933, Pt. 2; Pittard and Kaufmann, *Archiv. Suisses d'Anthrop. Gen.*, 1938, 8, 31; Brodie, A. G., *Amer. Jour. Anat.*, 1941, 68, 209 (head growth in children).

[11] Adair and Scammon, *Anat. Rec.*, 1930, 46, 349.

[12] Cave, A. J. E., *Jour. Anat.*, 1928, 68, 177; Stallworthy, J. A., *ibid.*, 1931, 67, 169; see also Limson, M., under note [6]; Edinger, Tilly, *Zeitsch. Anat. Entwickl.*, 1934, 102, 266 (evolution of parietal foramina).

[13] Bernstein, S. A., *Zeitsch. Anat. Entwickl.*, 1933, 101, 652; Sitsen, A. E., *ibid.*, 1933, 101, 120; *ibid.*, 1934, 103, 385; Leboucq and Seydel, *Ann. d'Anat. Path.*, 1932, 9, 654.

[14] Harris, H. A., *Bone Growth in Health and Disease*, 1933.

[15] Brash, J. C., *Edin. Med. Jour.*, 1934, 41, 305.

[16] Mortimer, H., *Radiology*, 1937, 28, 5.

[17] Murray, P. D. F., see note [10], p. 647.

[18] For a well reported case of microcephaly, see Cunningham and Telford Smith, *Trans. Roy. Soc. Dublin*, 1895, 8, 287.

[19] For irregular union of occipital and cervical segments, see references given in note [9], Chapter VI.

[20] Mall, F. P., *Amer. Jour. Anat.*, 1906, 5, 433; see also references given in preceding note [6].

[21] Another paired element which goes to make up the base of the vertebrate skull I have left unmentioned. This is the pair of *polar cartilages*, which appear on each side of the fenestra occupied by the pituitary. They appear to become fused in the intertrabecular plate.

[22] For the derivation of the ala temporalis, see Broom, R., *The Mammal-like Reptiles of South Africa*, 1932 (from the palato-quadrato bar); Kesteven, H. L., *Jour. Anat.*, 1927, 61, 111; *ibid.*, 1929, 63, 447; Fawcett, E., *ibid.*, 1910, 44, 303; De Beer, G. E., see reference given in note [1].

[23] Cope, V. Z., *Jour. Anat.*, 1917, 51, 127; van Gilse, P. H. G., *ibid.*, 1927, 61, 153.

[24] Cave, A. J. E., *Jour. Anat.*, 1931, 65, 363; Wrai, H., *Anat. Hefte*, 1907, 3, 33, 411; Limson, M., see note [6].

[25] See references given in note [9], Chapter X.

[26] Martin's *Lehrbuch der Anthropologie*, 1928.

[27] Thomson, Arthur, *Man's Cranial Form*, Oxford, 1903; Fischer, E., *Zeitsch. Morph. u. Anthropol.*, 1933, 31, 291.

[28] Keith, Sir A., *Jour. Anat.*, 1913, 47, 169; *Lancet*, 1911, 1, 903.

[29] Bayley, N., *Human Biology*, 1936, 8, 1; Abbie, A. A., *Jour. Anat.*, 1947, 81, 233.

[30] For relationship of sutural growth to cranial shape, see Mijsberg, W. A., *Zeitsch. Morph. Anthropol.*, 1932, 30, 535; Troitzky, W., *ibid.*, 1932, 30, 504; Peters, H. B., *ibid.*, 1932, 30, 317; Bolk, L., *Amer. Jour. Anat.*, 1915, 17, 495.

[31] Cameron, J., *Jour. Anat.*, 1929, 63, 413; also in succeeding volumes 1930-32.

[32] Mortimer, H., see under note [16]; Todd and Wharton, *Amer. Jour. Anat.*, 1934, 55, 97 (influence of thyroid); Dye and Kinder, *ibid.*, 1934, 54, 333 (influence of thyroid).

[33] See Martin's *Lehrbuch der Anthropologie*, 1928.

[34] Keith, Sir A., *Jour. Anat.*, 1910, 44, 251.

segment I have numbered 1 is that usually known as the premandibular, the real segment 1 being no longer represented in the human head. The palato-quadrato bar is a derivative of the mandibular segment and therefore should not have been given a separate segmental value, as has been done in Fig. 181.

[36] The late Prof. A. Brachet (*Traité d'Embryologie des Vertébrés*) regarded the prechordal part of the head with the prechordal foregut as the oldest parts of the human frame, the chordal segments of the skull and of the body being later additions. This is also the opinion of Prof. De Lange (see reference in note [1]). For a statement of Brachet's theory, see Woollard's *Recent Advances in Anatomy*, 1927; also *Jour. Anat.*, 1932, 66, 242.

[37] Gaskell, W. H., *Origin of Vertebrates*, London, 1910; see also Kingsbury and Adelman, *Quart. Jour. Mic. Sc.*, 1924, 68, 239.

CHAPTER XIII

DEVELOPMENT OF THE FACE

Evolution of the Human Face.—In our survey of the brain-containing part of the human cranium we have seen that its outstanding features are the result of a great cerebral development. When, however, we turn to the facial and pharyngeal parts of the skull and head, we find that the factors which have determined their shape are related to the functions of smell, respiration and of mastication. It is unnecessary to again insist on the fact that the human embryo, in the latter part of the first month, shows a resemblance to a generalized type of fish; it possesses the basis of a branchial arch system. As in the fish, the olfactory organ is represented by a pair of pits or depressions, which at first have

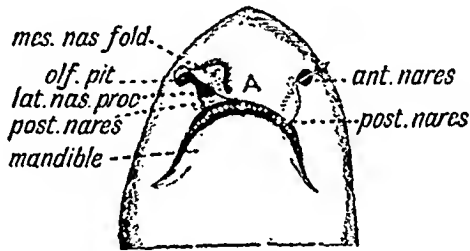


FIG. 182. The Naso-Buccal Grooves of a Dog-Fish. On the right side the naso-buccal channel is exposed.

no communication with the mouth. In some forms of fish—certain rays and sharks (Fig. 182)—a channel is formed between each olfactory pit and the mouth. The functional meaning of such a channel is evident: the water imbibed is sampled by the nose before entering the mouth. When pulmonary breathing was introduced, as in Dipnoean fishes, the open naso-buccal channel became enclosed by the union of its bounding folds. In amphibians, reptiles and birds the naso-buccal channel becomes dilated to form a true respiratory nasal passage, and the parts bounding the passage unite on the roof of the mouth to form the *primitive palate*. In Fig. 183 the parts entering into the formation of the primitive palate are shown. They are three in number: (i) a premaxillary and vomerine part developed between the nasal passages; (ii, iii) a right and left maxillary part, laid down on the lateral or outer aspect of each passage. In mammals a fourth element is added to the primitive or reptilian palate, and in this way the mammalian mouth is separated

from the nasal respiratory passage, and can serve the purposes of mastication and suction. Thus in the evolution of the face there have been three distinct stages: (i) a piscine, in which the nose and mouth were formed independently; (ii) an amphibian stage, where the nasal respiratory passage opened on the roof of the mouth; (iii) a mammalian stage, in which it opened in the naso-pharynx. In the development of the human embryo we see these three stages reproduced [1].

Processes which form the Face.—Towards the end of the 4th week of foetal life, five processes begin to spring from the base of the primitive cerebral capsule, which by the end of the 2nd month have completely united together to form the facial part of the head. In Fig. 184 a dia-

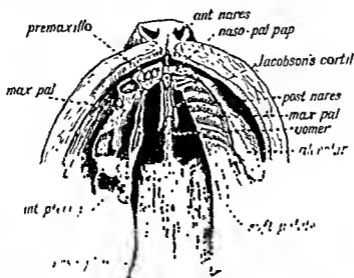


FIG 183 Roof of the Mouth of a Lion-Pap, showing the condition of cleft palate recalling in form the palate of reptiles. On the right side the bones are exposed by removal of the soft parts

grammatic representation is given of the condition of these five processes about the end of the 6th week of development. Of the five, one, the *nosol* or *fronto-nosol*, composed of symmetrical right and left halves, is median, and projects beneath the fore-brain; the others are lateral, two on each side, the *mandibulor* and *maxillary*. The cavity which these five processes surround is the *stomodaeum*, a space ultimately destined to form the nasal and part of the buccal cavities. The representatives of these five elements are recognizable in certain fishes (see Fig. 182). The part of the adult face formed by each process is shown in Fig. 185.

Nasal Region of Face.—In reality the core of the face is formed by the cartilaginous capsule which encloses the organ of smell. We have seen that the olfactory capsule occupies the terminal part of the prechordal plate, and in primitive vertebrates forms the entire snout or face (Figs. 160, 163). Hence the first step in the development of the human face

represents the upbuilding of the nasal cavities. Three stages in this process are depicted in Fig. 186. At the end of the 4th week the olfactory organ is exposed on each side of the fore-brain as a plaque surrounded by a growing raised margin or fold. The pituitary recess, opening from the stomodaeum (Fig. 186, *A*), lies in contact with the under surface of the fore-brain. At the end of the 6th week (*B*), the olfactory plaque has become a pocket by the upgrowth of the mesial and lateral nasal folds or processes, which, being united above, rise up as a hood. Below, the olfactory pit communicates with the buccal cavity by an open naso-buccal channel—just as in the dog-fish. At the same time the maxil-

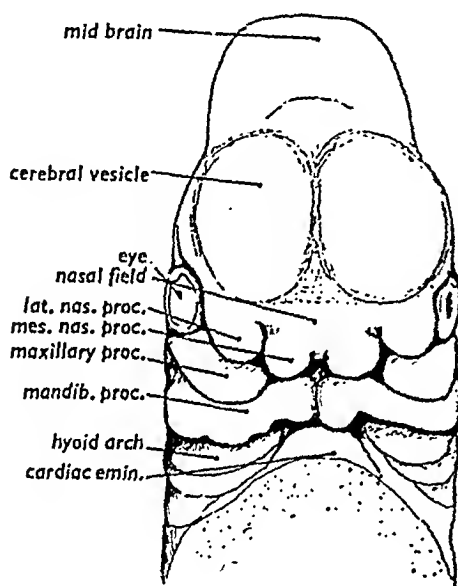


FIG. 184.

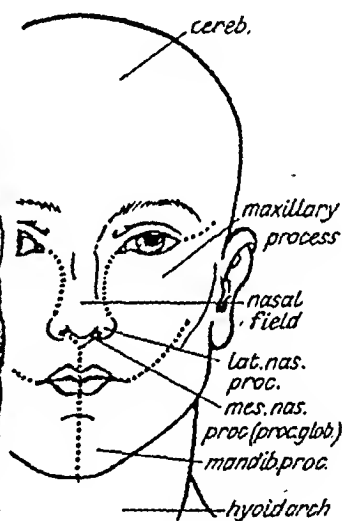


FIG. 185.

FIG. 184. Showing the formation of the Face by the Nasal, Maxillary and Mandibular Processes in an Embryo of the 6th Week. (After His.)

FIG. 185. Showing the Parts of the Face formed from the Nasal, Maxillary and Mandibular Processes.

lary process grows forward, and applies itself to and fuses with the substance of the lateral nasal fold. In the 7th week (*C*) the maxillary process has come in contact and is fusing with the globular end (globular process) of the mesial nasal fold, and thus the naso-buccal channel is covered over and we can now speak of anterior nares and a posterior opening or primitive choana—at first closed by an epithelial plug (Fig. 186, *C*). As the olfactory pockets enlarge they come closer together under the fore-brain until the mesial folds and the tissues between them form the primitive septum of the nose. Thus the nasal cavities which form the foundation of the face are built against the wall of the fore-brain and the nasal folds represent the margins of the outgrowing orifice.

We have been looking at the process of face building as seen on the

surface of the embryonic head; in Fig. 187, sections reveal the deeper changes which take place in the stages depicted in Fig. 186. The nasal

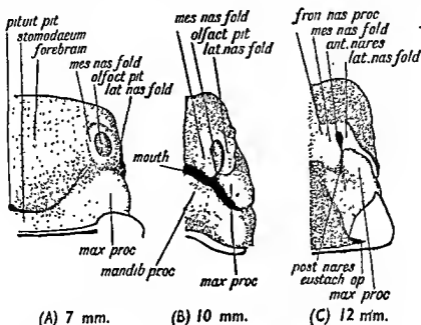


FIG. 186. Three stages in the formation of the Nasal Cavities and Primitive Palate. (Prof. J. E. Frazer.)

cavities, which are separated by a narrow septum in the adult, are set widely apart in the 6th week embryo (Fig. 187, *A*), being separated by

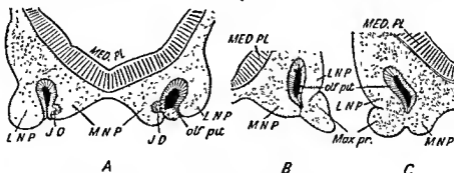


FIG. 187. Sections across the Embryonic Head to show the growth of the processes which enclose the Nasal Pockets. (After Veau and Politzer.)

A. Of an embryo early in the 6th week of development.

B. Late in the 6th week.

C. Early in the 7th week. In *B, C* only half of the head is depicted.

olf. pit, olfactory pocket or cavity; *M.N.P.*, mesial nasal process; *L.N.P.*, lateral nasal process; *Max. pr.*, maxillary process; *J.O.*, epithelium destined for Jacobson's organ; *MED. PL.*, medullary plate of fore-brain.

a flat field or process, the *fronto-nasal*. At each side of this field there rise up two minor processes, the *mesial nasal*, enclosing the olfactory pocket on its inner side (Fig. 187, *M.N.P.*). At the outer side of each

represents the upbuilding of the nasal cavities. Three stages in this process are depicted in Fig. 186. At the end of the 4th week the olfactory organ is exposed on each side of the fore-brain as a plaque surrounded by a growing raised margin or fold. The pituitary recess, opening from the stomodaeum (Fig. 186, *A*), lies in contact with the under surface of the fore-brain. At the end of the 6th week (*B*), the olfactory plaque has become a pocket by the upgrowth of the mesial and lateral nasal folds or processes, which, being united above, rise up as a hood. Below, the olfactory pit communicates with the buccal cavity by an open naso-buccal channel—just as in the dog-fish. At the same time the maxil-

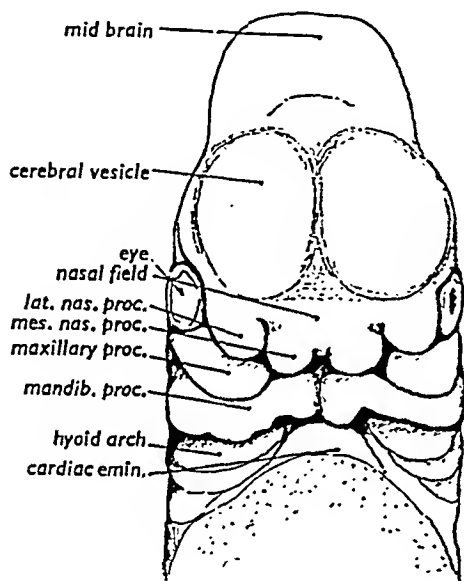


FIG. 184.

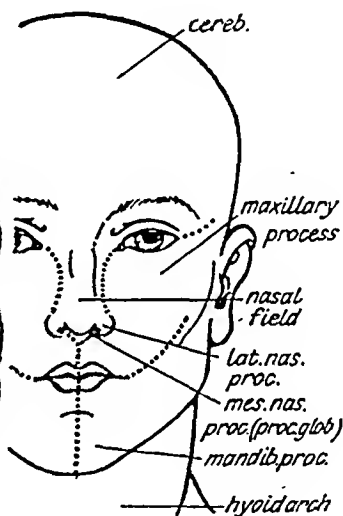


FIG. 185.

FIG. 184. Showing the formation of the Face by the Nasal, Maxillary and Mandibular Processes in an Embryo of the 6th Week. (After His.)

FIG. 185. Showing the Parts of the Face formed from the Nasal, Maxillary and Mandibular Processes.

lary process grows forward, and applies itself to and fuses with the substance of the lateral nasal fold. In the 7th week (*C*) the maxillary process has come in contact and is fusing with the globular end (globular process) of the mesial nasal fold, and thus the naso-buccal channel is covered over and we can now speak of anterior nares and a posterior opening or primitive choana—at first closed by an epithelial plug (Fig. 186, *C*). As the olfactory pockets enlarge they come closer together under the fore-brain until the mesial folds and the tissues between them form the primitive septum of the nose. Thus the nasal cavities which form the foundation of the face are built against the wall of the fore-brain and the nasal folds represent the margins of the outgrowing orifice.

We have been looking at the process of face building as seen on the

will unite and form the whole of the upper lip and an entire palate (Fig. 201) [4]. Any of these processes may be under or over-developed ;



FIG. 189.

FIG 189. Face of a Child showing the left Nasal Process and Pocket as a free Polypoid Body and the left Maxillary Process ununited with the Mesial Nasal (left hare lip). (After Kirchmayer.)

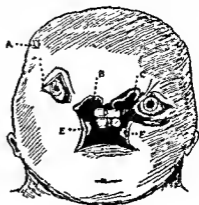


FIG. 190.

FIG. 190. Face of Child in which the Nasal and Maxillary Processes are ununited.

A
nasal
body

over-development of the nasal and under-development of the mandibular (micrognathia) are of common occurrence.

The cleft in the lip of the hare is exactly in the middle line, and separates

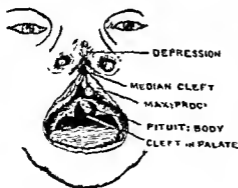


FIG. 191

FIG. 191 Median Hare Lip in a Child with Partial Cleft Palate and Ectopia of the Pituitary. (Mr A. R. Tweedle's case.)

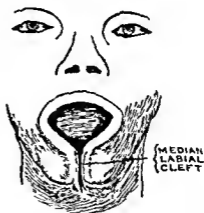


FIG. 192.

FIG. 192 Median Cleft of the Lower Lip and Jaw. (MacCormick's case.)

the right from the left maxillary process, the mesial nasal being much reduced and buried in the cleft. The upper lip and septum of the nose may be cleft in the mid-line. This is due to a failure in the approximation of the mesial nasal processes. In the case shown in Fig. 191, there was a partial cleft of the palate, and the pituitary formed a

pocket there is also rising another enclosing process or fold, the *lateral nasal (L.N.P.)*. A few days later (Fig. 187, *B*) the maxillary process has grown against and united with the two nasal processes, thus completing the wall of the nasal pocket. Early in the 7th week (Fig. 187, *C*) the three processes are seen to be more widely united. The olfactory cavity is now deeply embedded; the inter-olfactory or septal field becomes relatively narrower and its distal or buccal end is carried further and further from the brain cavity. By the end of the 7th week (Fig. 188, *A*) anterior nares and septum become recognizable.

Upper Lip.—The account given here of the formation of the upper lip is based on Prof. J. E. Frazer's investigations, Figs. 188, *A*, *B*, being borrowed from him. It will be observed that the right and left maxillary processes, after coming in contact with the terminal ends of the mesial

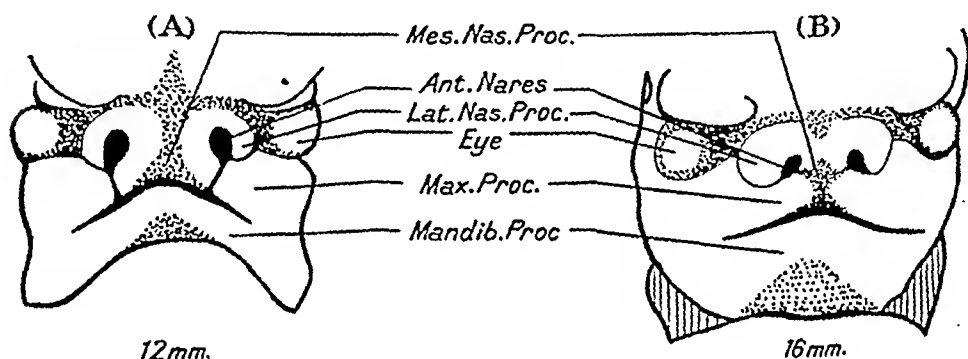


FIG. 188.

A. The Upper Lip in the 6th week.

B. The Upper Lip in the 7th week. (After Frazer.)

nasal processes (Fig. 188, *A*), proceed to invade and overwhelm them, so that ultimately the maxillary processes meet in the median groove or philtrum of the upper lip. The muscular and vascular tissues of the upper lip are carried to the mid-line by the invasive maxillary tissues [2].

Malformations of the Face.—These processes may fail to unite in the 2nd month, and in this manner malformations of the face are produced [3]. The most common anomaly is a partial failure of the nasal and maxillary processes to fuse, various degrees of *hare lip* and *cleft palate* being thus caused. In *hare lip* the cleft appears in the upper lip between the maxillary elements and also between the maxillary and the mesial nasal. In *cleft palate* the failure of union occurs between the deep parts of the mesial nasal and maxillary processes (Fig. 183). The lateral or the mesial parts of the nasal process may fail to fuse with the maxillary processes, and appear on the face as polypoid or irregular projections separated by deep clefts (Figs. 189, 190). Or the nasal processes may be absent and then the right and left maxillary processes

facial processes fails to take place, then subsequent growth tends to move the processes apart, and union becomes impossible. The cleft in the lip or palate increases in width as the foetus becomes older. The tongue lies between the maxillary plates (Fig. 194), a normal position during the 2nd month. It is extruded as the palate is formed, the extrusion being made possible by the rapid growth of the mandibular and maxillary processes in the earlier part of the 3rd month [3].

Structures formed in the Mesial Nasal Processes.—We have already seen that the mesial nasal processes, which represent the inner walls of the nasal pockets or cavities, grow out from the base of the fore-cranium, and when they coalesce to become the primitive septum of the nose, the cartilage formed in their united substance represents a direct forward continuation of the trahecular plate. From the united substance of

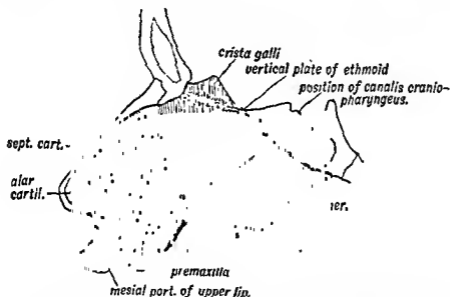


FIG. 195. Showing the structures formed in the Mesial Nasal Processes. Only part of the premaxillary and a buried part of the upper lip are formed in the mesial processes.

the mesial nasal processes are formed the septum of the nose (Fig. 195), the medial element of the premaxillary part of the palate, and the frenum and buried median part of the upper lip (Figs. 184, 185, 188). Part of the cartilage of the septum remains unchanged as the *septal cartilage* (Fig. 195). In the septal wall are also developed the mesial limbs of the *alar cartilages*, which give form to the anterior nares. One element is added to the lower anterior part of the septum—just above the opening of the naso-palatine canal—the *paraseptal cartilages* (Fig. 183), which primarily serve for the protection of an isolated area of the olfactory membrane—*Jacobson's organ*—reduced to a mere vestige in man (Fig. 187, A). In Fig. 186, C, it will be observed that the lateral

tumour-like mass within the septum of the nose. A median cleft in the lower lip is also rare, and is due to a failure in the union of the right and left mandibular processes of the lower jaw, which should unite in the 6th week (Fig. 192). Sometimes children are born with two noses—a right and a left, each with two narial openings. The chin and the tongue may be duplicated. Another remarkable condition, *cyclopia*, is shown in Figs. 201, 242, where the nasal processes have united together to form a single proboscis-like structure projecting above the eyes, these being partly fused. In this condition the palate and upper lip are formed by the union of the maxillary processes. The result illustrates how adaptable the various embryological parts of the face are. *Cyclopia*

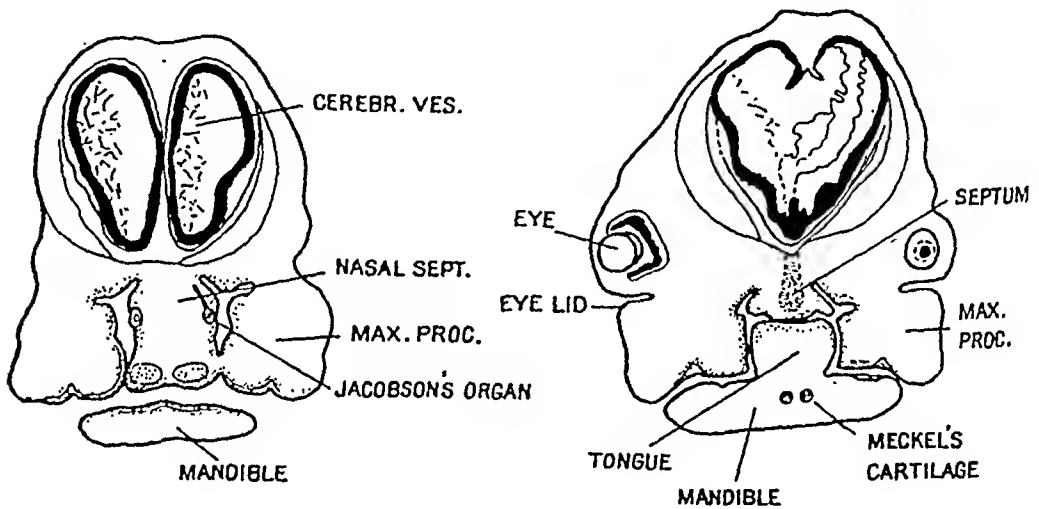


FIG. 193.

FIG. 194.

FIG. 193. Coronal section of the Head of a Human Embryo in the 6th week of development and 14 mm. long. (After J. L. Paulet.)

FIG. 194. Similar section of the same Embryo further back, showing the Tongue in the Palatal Cleft. (J. L. Paulet.)

assumes many forms and as already mentioned (p. 71) is the result of damage done to the cranial part of the medullary plates in their earliest development [5].

Method of Fusion.—The manner in which embryological parts unite is similar in nature to the healing of wounds. Fig. 193 represents a coronal section of the head of a human embryo, in which the mesial nasal process containing the germinal epithelium of the upper incisor teeth is about to unite with the maxillary. The ectodermal coverings of the processes are in contact. Across the epithelial union thus formed the mesodermal tissue spreads, the two processes thus becoming intimately united. We know that the process of healing may be arrested by many pathological conditions; the process of embryological union also may be arrested, but the exact causes of the arrest we do not yet know. If union of the

canines begin to develop they fuse with the maxillae. The premaxilla is more reduced in man than in any other primate; in him it is partly fused with and overlapped by the maxilla almost from the first appearance of their centres of ossification; in apes fusion does not occur until the eruption of the permanent teeth. The vestigial character of the premaxilla in man is due to the reduced size of his masticatory apparatus and the consequent retrogression in the development of the facial part of the skull. The reduction of the premaxillary element alters the sill of the nasal aperture [7].

Since the preparation of the last edition (1933), publications by Prof. Wood-Jones and his pupils and by Prof. Ashley-Montagu compel me to

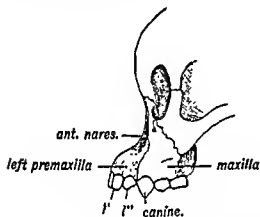


FIG. 197.

FIG. 197. Showing the suture on the face between the premaxilla and maxilla in the Skull of a Young Orang.

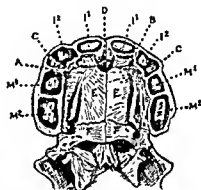


FIG. 198.

FIG. 198. Diagram of skull showing sutures between maxilla and premaxilla. On the

alter my account of the formation of the premaxilla [8]. As readers will learn at a glance from Fig. 207 (p. 251) I then held the accepted opinion that this bone arose as one piece within the mesial nasal process. As will be seen from Fig. 199, *A*, the premaxilla is made up of two elements, a mesial element (*premax. b.*), which is finely stippled in Fig. 199, *A*, and is seen to lie between the alveoli for the incisor teeth and the nasopalatine canals. The other or lateral element (*pre-max. a.*) forms the outer wall of the incisive alveoli and all the bone lying between these alveoli and the nasal sill. This second or lateral element of the premaxilla is derived from the mesoderm of the maxillary process and is added to the mesial element when the maxillary process becomes joined to the mesial nasal in the 6th week. The lateral element carries its own nerve and blood supply from the maxillary process. The artery and accompanying nerve descend, as Prof. Wood-Jones has vividly

nasal process also fuses with the mesial; the paraseptal cartilages are derived from the lateral nasal processes (Fawcett).

The *vomer* is developed in the membrane (perichondrium) which covers the primitive septum (Fig. 204). A centre of ossification appears at the end of the 2nd month on each side near the lower border of the septum; these fuse together under the palatal margin of the cartilage. Thus the vomer forms at first a shallow trough in which the cartilage of the septum appears to be implanted (Fig. 196). At its anterior end a cartilaginous element comes to be included—a derivative of the anterior paraseptal cartilages (Fawcett).

The *Vertical Plate of the Ethmoid* is formed by a direct ossification of the cartilage of the primitive septum. Ossification begins in the 4th month. The crista galli, the intra-cranial part of the septum, is formed in part by ossification proceeding into the attachment of the falx cerebri.

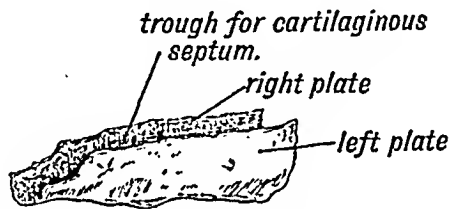


FIG. 196. Showing the Trough-shaped Vomer of the newly born.

Premaxillary Bones.—The right and left premaxillary bones carry the four upper incisor teeth. At birth the suture between the premaxilla and maxilla can be seen on the hard palate; it runs on each side from the naso-palatine foramen to the alveolus between the lateral incisor and canine (Fig. 198). As is shown in that illustration, the relationship of this suture to the tooth sockets is variable, but the relationship just mentioned is the usual one. On the facial aspect, the suture between the premaxilla and maxilla disappears very soon after separate centres of ossification have appeared for these two bones. The centres appear late in the 7th week, the maxillary centres preceding those for the premaxillae. The nasal spine is formed by the premaxillae. The median or septal processes of the premaxillae represent the prevomers which are seen as distinct bones in the primitive palate of amphibia. Prof. Fawcett found that these processes have separate centres of ossification in man [6].

In mammals generally the premaxillae are highly developed, separated throughout their whole extent by a suture from the maxillae, and form the snout part of the face. In the higher Primates the face becomes less elongated, less *prognathous*, or projecting, and the premaxillae less developed. In the orang, for instance, the premaxillary sutures are distinctly seen on the face at birth (Fig. 197), but as the permanent

maxillary and premaxillary parts of the upper jaw. This suture disappears prematurely in the human maxilla because of two circumstances: the maxilla and premaxilla serve as a functional whole; in the widening of the nasal aperture new bone is deposited on the facial aspect of the bone, while absorption is taking place on its nasal aspect. Hence the premaxillary boundary is preserved longer on the mesial than on the lateral aspect of the bone (Fig. 200, B).

Relationship of the Premaxilla to Cleft Palate.—It is usual for the sockets of all four incisor teeth to be formed in the premaxilla (Figs. 197, 207). In many cases of cleft palate only the two central incisors are situated on

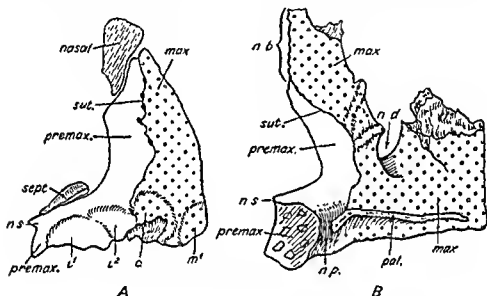


FIG. 200.

A Lateral aspect of the Maxilla of a 6 months Foetus in which the suture (*Sut.*) separating the premaxilla is still evident (Felber)

B Mesial aspect of the Maxilla of a full-time Negro Foetus in which the suture (*Sut.*) separating the premaxilla is unusually well preserved (Ashley Montagu)

n.s., nasal spine; *sept.*, septal process of premaxilla; *l¹*, alveolus for 1st incisor; *l²*, for 2nd; *c.*, for canine; *m¹*, for 1st milk molar; *n.p.*, naso-palatine opening; *pal.*, palate; *n.d.*, nasal duct; *n.b.*, nasal border.

the premaxilla, the sockets of the lateral incisors being attached to the maxilla. Even in the normal palate (Fig. 198) this may be the case. Cleft palate is due not to a failure of ossific centres to join but to a non-union of two embryological masses—the mesial nasal and maxillary. The germ or bud of the lateral incisor is formed at the point of union of the mesial nasal and maxillary processes. If these processes fail to join, the bud of the lateral incisor, as the processes move apart during subsequent growth, may be carried away by the maxillary or premaxillary element, or, as I have seen, be left stranded in the cleft between the processes. If the lateral incisor remains attached to the maxillary process, then its socket is formed by that element; if by the premaxillary,

described [9], in a canal on the nasal aspect of the ascending process of the maxilla, until the narial sill is reached, where the main termination crosses to the nasal septum, while branches are sent to furnish the upper incisors with arteries and nerves (the anterior dental). Evidence in support of the dual origin of the premaxilla is furnished by two kinds of malformation. There is first that in which the maxillary process fails to reach and fuse with the mesial nasal process (Fig. 202); here the incisor teeth are destitute of their arteries and nerves and are usually excised by the surgeon when he seeks to restore the palate. Then there

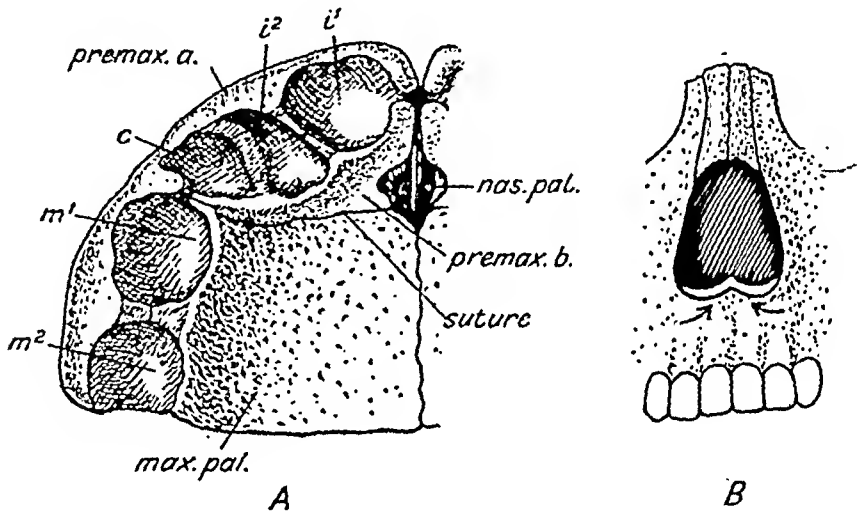


FIG. 199.

- A. Half of the Palate of a Foetus in the 6th month of development to show the two elements concerned in the formation of the premaxilla. The area (finely stippled) lying between the incisive alveoli and the naso-palatine opening (*pre-max. b.*) is formed in, and derived from, the mesial nasal process; but the part (coarsely stippled) which forms the anterior wall of the incisive alveoli and all the bone between these alveoli and the narial opening is derived from the maxillary process (*pre-max. a.*). The rest of the palate, formed by the maxilla, is coarsely stippled. (After O. Norberg.)
- i*¹, alveolus for 1st incisor; *i*², alveolus for 2nd incisor; *c*, for canine; *m*¹, 1st milk molar; *m*², 2nd milk molar; *nas. pal.*, opening of naso-palatine canals; *max. pal.*, maxillary palate.
- B. Facial aspect of an adult skull to illustrate the submergence of the premaxilla by maxillary overgrowth as postulated by Prof. Wood-Jones. The maxillary area is stippled. The arrows show the direction of the overgrowth. (E. H. Johnson.)

is the other kind of malformation, of which two cases have been reported by Prof. Derry [10], where the mesial element has failed to form, but the maxillary or lateral element has been developed, meeting the other maxillary element in the mid-line and forming a floor for the nasal opening. The dual composition of the premaxilla holds true for all primates; it is not confined to man. Indeed, the greater part of the primate premaxilla is derived from the substance of the maxillary process [11].

In Fig. 200, A, is reproduced a drawing of an exceptional foetal human maxilla, which, at the 6th month preserves the suture between the

maxillary and premaxillary parts of the upper jaw. This suture disappears prematurely in the human maxilla because of two circumstances: the maxilla and premaxilla serve as a functional whole; in the widening of the nasal aperture new bone is deposited on the facial aspect of the bone, while absorption is taking place on its nasal aspect. Hence the premaxillary boundary is preserved longer on the mesial than on the lateral aspect of the bone (Fig. 200, *B*).

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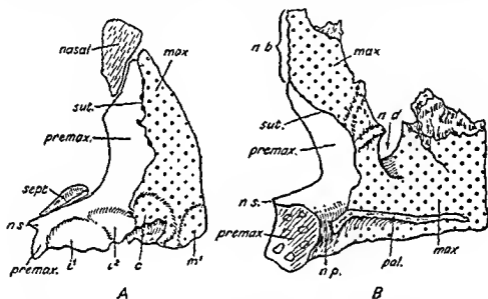


FIG. 200.

A. Lateral aspect of the Maxilla of a 6 months Foetus in which the suture (Sut.) separating the premaxilla is still evident. (Felber.)

B. Mesial aspect of the Maxilla of a full-time Negro Foetus in which the suture (Sut.) separating the premaxilla is unusually well preserved. (Ashley Montagu)

ns, nasal spine; *sept.*, septal process of premaxilla; *i*¹, alveolus for 1st incisor, *i*², for 2nd; *c*, for canine; *m*¹, for 1st milk molar; *ns*, naso-palatine opening; *pal*, palate; *nd*, nasal duct; *nb*, nasal border.

the premaxilla, the sockets of the lateral incisors being attached to the maxilla. Even in the normal palate (Fig. 198) this may be the case. Cleft palate is due not to a failure of ossific centres to join but to a non-union of two embryological masses—the mesial nasal and maxillary. The germ or bud of the lateral incisor is formed at the point of union of the mesial nasal and maxillary processes. If these processes fail to join, the bud of the lateral incisor, as the processes move apart during subsequent growth, may be carried away by the maxillary or premaxillary element, or, as I have seen, be left stranded in the cleft between the processes. If the lateral incisor remains attached to the maxillary process, then its socket is formed by that element; if by the premaxillary,

then the cleft appears in the more usual situation, and the socket forms part of the premaxilla. The late Mr. Clement Lucas observed that the lateral incisor is often small or even absent in families subject to cleft palate.

Naso-palatine Foramen.—The naso-palatine foramina are formed where the mesial nasal and two maxillary processes unite to form the *palate* (Fig. 207). In animals with well-developed premaxillae the two naso-palatine (anterior palatine) foramina are large, and through each passes the naso-palatine duct, which allows a communication between the buccal and nasal cavities. It is tempting to think that the odour of the food within the mouth may thus reach the organ of Jacobson, which

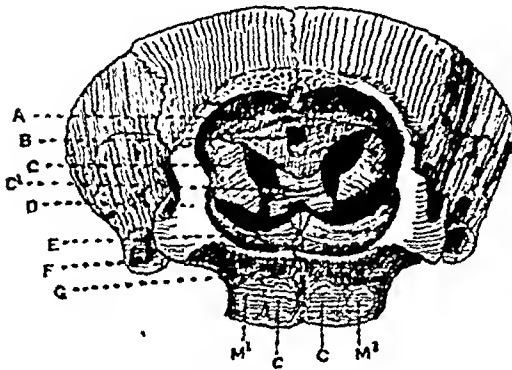


FIG. 201.

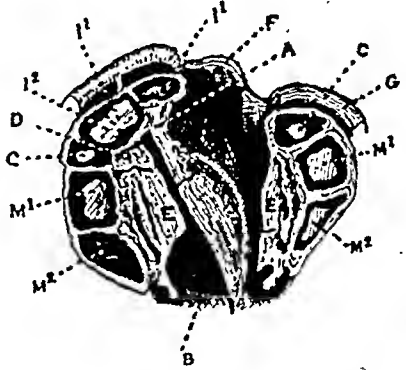


FIG. 202.

FIG. 201. Facial part of the Skull of a Cyclops Foetus, in which the nasal processes formed a free proboscis, the eyes a median structure and the maxillary processes the palate. A, orbital plates of frontal; B, fused optic foramina; C, orbital plate of sphenoid; C¹, basal-sphenoid; E, orbital plate of maxilla; F, ear; G, superior maxilla; C, canine; M¹, 1st milk molar.

FIG. 202. Case of Cleft Palate, in which the maxillary and premaxillary processes have remained ununited on the left side. A, septal process of the inner or mesial element of the premaxilla; B, nasal septum; C, canine; D, palatal process of premaxilla; E, palatal process of maxilla. The left lateral incisor was absent.

is situated on the septum, close to the nasal orifice of the duct, but the evidence goes against such a supposition [12]. In man the upper ends of the ducts remain open; they terminate blindly below, behind the mesial incisor teeth, in the naso-palatine or incisive papilla.

Nasal Duct.—The lachrymal sac and nasal duct, through which tears pass from the eye to the inferior meatus of the nasal cavity, are formed between the lateral nasal and maxillary processes (Figs. 185, 186, 190). At the end of the 6th week, when the furrow between the maxillary and nasal processes is obliterated, the nasal or naso-lachrymal duct is represented by a solid bud or core of ectoderm embedded at the inner angle of the eye and in the site of the upper part of the naso-maxillary groove or fissure. This bud becomes cord-like, one extremity growing towards the nasal cavity, which it reaches at the beginning of the 3rd month,

while the orbital extremity expands to form the lachrymal sac. The canaliculization of the duct begins in the 3rd month, but is not complete until late in foetal life. In Fig. 190 the lateral nasal and maxillary processes have not fused; the eye is separated from the nasal cavity by two folds; the outer represents the semilunar fold, the inner a fold in which the lachrymal canaliculi and caruncula lachrymalis are formed [13].

Structures formed in the Lateral Nasal Process.—The lateral nasal process is developed to form the outer wall and roof of the chamber containing the olfactory organ. Within it develops a plate of cartilago

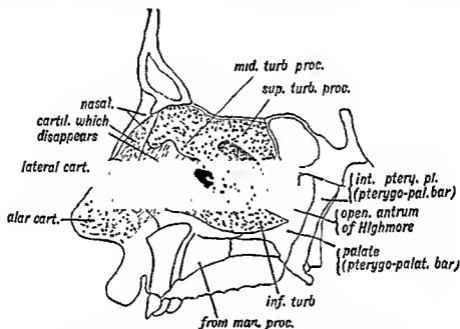


FIG. 203. Showing the structures formed in the Lateral Nasal Processes

which represents the greater part of the cartilaginous olfactory capsule of lower vertebrates. In the human embryo the process of chondrification begins near its lower border and spreads up towards the roof (Frazer), where it joins the upper edge of the septal cartilage, developed in the united mesial nasal processes, and also spreads backwards to enfold the hinder part of the olfactory chamber and to become continuous with the presphenoid part of the trabecular plate. The cribriform area is the last to be formed (see Figs. 174, A, B, p. 221). In front, the lower border of the lateral nasal process joins the septal process, adding to it the paraseptal cartilage (p. 241).

The Cartilage of the Lateral Nasal Process (Fig. 203) forms :

(i) The cribriform plate around the olfactory nerves as they issue from the olfactory bulb;

(ii) The lateral mass of the ethmoid, at first merely a plate of cartilage; the superior and middle turbinate processes are developed from the plate (Fig. 204); ossific centres appear in the cartilage of the lateral mass and turbinate processes during the 4th month of foetal life;

(iii) The inferior turbinate bone (Fig. 204) (maxillo-turbinal). The body of the superior maxilla is developed on its outer side in the maxillary process (Fig. 204);

(iv) The lateral and part of the alar cartilages of the nose (Fig. 203);

(v) In the membrane over the cartilage, between the ethmoid behind and the cartilages of the nares in front, are developed the lachrymal and nasal bones, and the ascending processes of the superior maxilla and

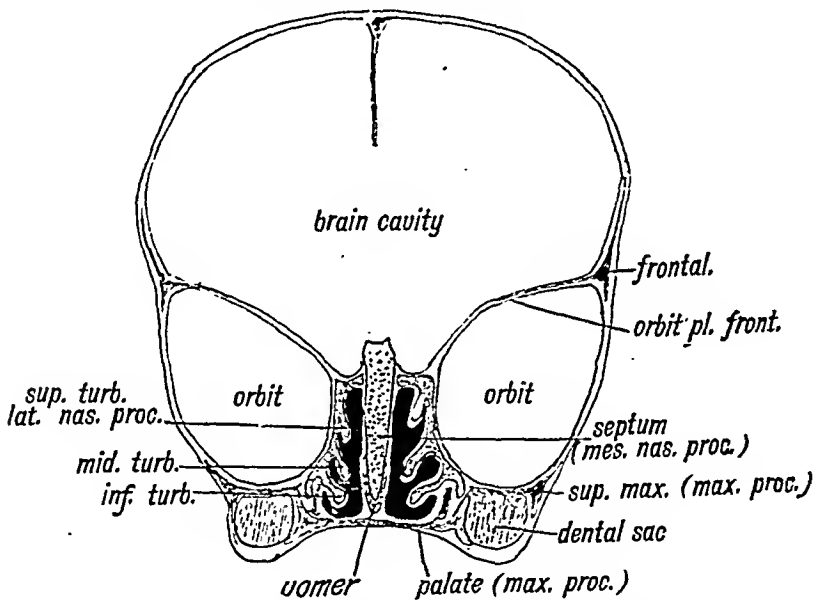


FIG. 204. Coronal section of the Skull of a 7th-month Human Foetus to show the cartilages of the Lateral and Mesial Nasal Processes and the bones formed round them.

premaxilla. The cartilage beneath these bones disappears after birth. Ossification of the nasal bone appears at the beginning of the 3rd month; the centre for the lachrymal appears late—at the beginning of the 4th month (Mall).

Arteries and Nerves of the Nasal Processes.—A knowledge of the development of the face assists one to unravel the complicated distribution of its arteries and nerves. Each process carries its own vessels and nerves.

1. **Mesial Nasal Process.** The chief artery and nerve of this process are the naso-palatine, but branches also come from the nasal nerve and its accompanying artery, the anterior ethmoidal.

2. **Lateral Nasal Process.** The nerves of the lateral nasal process are derived from Meckel's ganglion and from the descending palatine nerve.

Vessels accompany these nerves from the descending palatine artery. The nasal nerve and anterior ethmoidal artery supply the process in front.

Visceral Mesoderm.—The nasal processes spring directly from the cranial capsule and the mesoderm which makes up their substance is derived therefrom (Fig. 187, p. 237). We now pass to consider parts of the face derived from two other processes—the maxillary and mandibular. Their mesoderm is of a different origin: they belong to the visceral arch series; their mesoderm is visceral in origin (see p. 229). The maxillary and mandibular processes carry mesoderm of this origin into the composition of the face [14].

Parts formed from each Maxillary Process.—The maxillary process

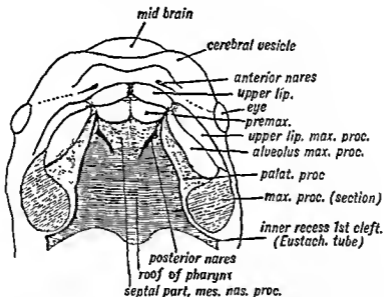


FIG 205 Showing the ingrowth of the Palatal Plates of the two Maxillary Processes at the end of the 6th week. The openings indicated as "posterior nares" are the primitive posterior nares or choanae. (After Kollmann)

springs from the base of the mandibular process at the end of the 4th week of development, and sweeping forwards below the eye, separates that structure from the mouth (see Figs 60, 61, 185). In front it comes in contact and fuses with the lateral nasal process, which it assists to form the outer wall and floor of the nasal cavity, and, in the 7th week, with the globular enlargements of the mesial nasal process. The maxillary processes also provide the mesoderm of the lateral element of the premaxilla and also that which invades and gives substance to the upper lip. The part of the face formed by the maxillary process is shown in Fig. 185. The hard palate (with the exception of the premaxillary part) is formed by a *palatal plate* which begins to grow inwards from the maxillary process in the 6th week (Fig. 205) and fuses with the plate of the

opposite side about the 10th week [15]. The palatal processes separate the buccal from the nasal cavities, forming the roof of the one and the floor of the other. The palatal plates meet first with the premaxillary part (Fig. 206); behind that they come in contact with each other; the process of fusion spreads backwards, and before the end of the 3rd month the hard and soft palates form a complete naso-buccal septum.

Cleft Palate [3].—To understand the manner in which the various forms of clefts arise in the palate it is necessary to note the manner in which the septum of the nose grows and the fate of the primitive posterior nares or choanae. At the end of the 6th week (Fig. 205) the nasal septum is seen to be relatively short and wide and to form the mesial borders of the primitive choanae. By the 9th week (Fig. 206) the septum

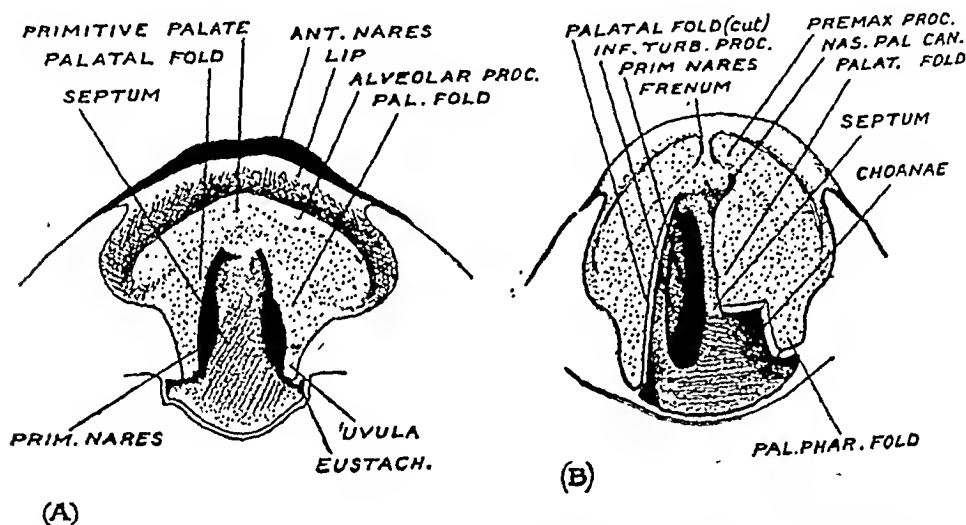


FIG. 206. Development of the Maxillary Palate. *A*, stage reached in 9th week; *B*, schematic figure to illustrate the manner in which the maxillary folds are applied to the nasal septum. (Prof. Frazer.)

has grown greatly in length, pushing the primitive palate forwards away from the base of the skull, and thus presenting a long posterior or palatal border which still forms the mesial edges of the primitive choanae; the choanae still extend from the primitive palate to the sphenoidal end of the septum. The dorsum of the foetal tongue lies against the lower or free margin of the septum with the palatal folds tucked under its lateral margins (Fig. 194) until the 9th week, when the forward growth of the primitive palate lifts the nasal septum off the dorsum of the tongue and allows the palatal folds to come in contact with each other and with the lower margin of the septum. The manner in which the palatal folds are applied to the septum is shown in Fig. 206, *B*; by a process akin to the healing of wounds the palatal folds unite with each other and with the palatal border of the septum. The process begins at the pre-

maxillary end and passes backwards, but the posterior part of the septum is left free to form the partition between the permanent posterior nares. Thus in the formation of the palate a Y-shaped cleft has to be united; the short limbs lie on each side of the premaxilla in the primitive palate, the long limb in the middle line of the permanent or mammalian palate. All three parts may remain ununited, as in Fig. 190, or the long limb with one short, as in Fig. 202, or only the long limb, as in Fig. 183. Further, it sometimes happens that one or both primitive choanae are closed permanently by the plug of epithelium, which temporarily occludes them, becoming organized and forming membrane or bone. As the septum and choanae expand this occluding membrane or partition, if it persists, is stretched and gives rise to *atresia of the posterior nares*.

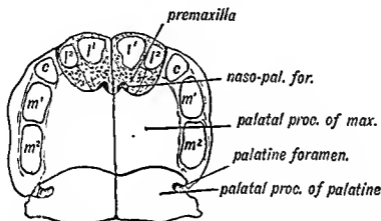


FIG 207. The Hard Palate at Birth, illustrating the discarded view that the whole of the premaxillary area was formed in the mesial nasal process (Compare with Fig 199)

The wide gap and bent septum seen in nearly all cases of cleft palate are due to changes produced by growth in the later months of foetal life. An asymmetrical growth is a result of the failure in the union of the processes (see note [3]).

Soft Palate.—While the hard palate is derived from the palatal plates of the maxillary processes, the soft palate (Fig. 206, *A*) is derived from a fold which arises as a prolongation backwards of each horizontal plate into the pharynx [16]. Into the *palatal folds* spread derivatives of the superior constrictor to form the palato-pharyngeus, palato-glossus and azygos uvulae, and possibly also the levator palati. The posterior pillars of the fauces are continuations of the palatal folds within the pharynx. A divided uvula represents a failure of the final stage in the formation of the palate.

Bones formed in each Maxillary Process.—The zygomatic process of the temporal, the malar, the lateral element of the premaxilla, and the

greater part of the superior maxillary are formed directly in the connective tissue within the process. They are membrane-formed or *dermal* bones. The centres for the maxilla appear at the beginning of the 7th week in the parts of the process which lie above the alveolar margin and under the eye. Very soon, after the various processes of the face are fully united, an extension passes upwards over the lateral nasal cartilage towards the frontal bone (frontal process); the orbital, alveolar, and palatal processes are later extensions from the two original centres of ossification.

Palato-Quadrate Bar.—The substance of the maxillary process not only spreads forwards into the face but sends upwards an extension on the side of the head. In this temporal extension is developed the squamous part of the temporal bone and also the muscles of mastication.

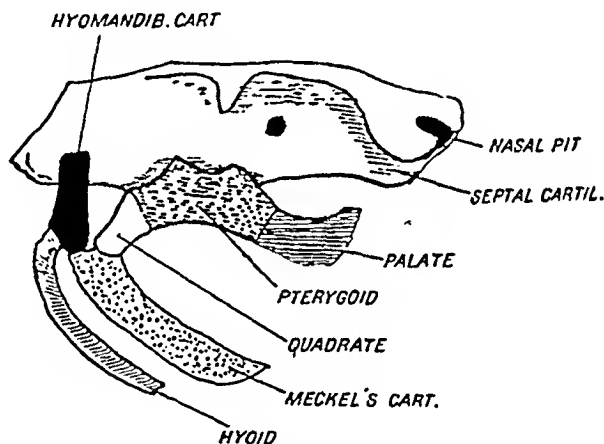


FIG. 208. The Cartilages in the Nasal, Maxillary, Mandibular and Hyoid Processes of a Shark.

tion [17]. In lower vertebrates the maxillary process is supported by a skeletal bar of cartilage known as the palato-quadrate bar, because it stretches from the palate to the quadrate bone; it springs from the base of the mandibular arch (Fig. 208). Although in the human embryo this cartilaginous bar is at no time clearly differentiated (Fawcett), there can be no doubt that two bones have arisen in connection with it—namely the palate and internal pterygoid (Fig. 209). The internal pterygoid plate—the first part of the sphenoid to ossify—is formed early in the 3rd month in membranous tissue which overlies the position of the middle part of the bar, while the vertical plate of the palate is developed in membrane over its more anterior part. Ossification extends to the horizontal plate, within the horizontal plate of the maxillary process, at the end of the 2nd month. The great wing of the sphenoid is also a derivative of this bar (p. 221).

The mandibular process has also a cartilaginous bar developed within

it known as *Meckel's cartilage*. Thus each of the processes which grow out to form the face has a basis of cartilage, but while the cartilages within the nasal processes are continuous with the base of the skull, the cartilage within the maxillary process comes in contact by its posterior extremity with Meckel's cartilage (Fig. 208). The quadrate bone, which is well seen as a separate element in birds and reptiles, forms a movable base on which the lower jaw articulates. This form of joint gives birds and reptiles an easy faculty of swallowing unmasticated food. With the development of grinding and chewing teeth in the very early ancestry of mammals a more stable form of temporo-mandibular articulation was evolved, the mandible during the change coming to articulate with the temporal bone, thus leaving the upper end of Meckel's cartilage

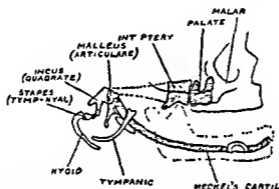


FIG. 209 Diagram to show the position of the bones in the Skull of the Human Foetus which are formed in connection with the palato-quadrate bar.

and the quadrate free to be utilized as the malleus and incus by the organ of hearing [18].

The simplest condition of the cartilages of the maxillary and mandibular processes is seen in certain fishes. In the common base of these two processes, there is developed a cartilage which binds the basal ends of the palato-quadrate bar and Meckel's cartilage to the skull (Fig. 208). The cartilage of the hyoid arch is also bound to it, and hence it is known as the *hyo-mandibular cartilage*.

Nerves and Arteries of the Maxillary Process.—A knowledge of the manner in which the maxillary process is developed explains the distribution and course of its arteries and nerves. The second division of the 5th, represented by the infra-orbital, descending palatine, pterygo-palatine, and Vidian nerves, forms its nerve supply. Nerves and vessels are carried to the upper incisors and their alveoli by the lateral pre-maxillary element. The main artery is the internal maxillary. The temporal artery supplies the temporal extension. It is probably in connection with this extension that a very strange thing happens in

greater part of the superior maxillary are formed directly in the connective tissue within the process. They are membrane-formed or *dermal* bones. The centres for the maxilla appear at the beginning of the 7th week in the parts of the process which lie above the alveolar margin and under the eye. Very soon, after the various processes of the face are fully united, an extension passes upwards over the lateral nasal cartilage towards the frontal bone (frontal process); the orbital, alveolar, and palatal processes are later extensions from the two original centres of ossification.

Palato-Quadrate Bar.—The substance of the maxillary process not only spreads forwards into the face but sends upwards an extension on the side of the head. In this temporal extension is developed the squamous part of the temporal bone and also the muscles of mastication.

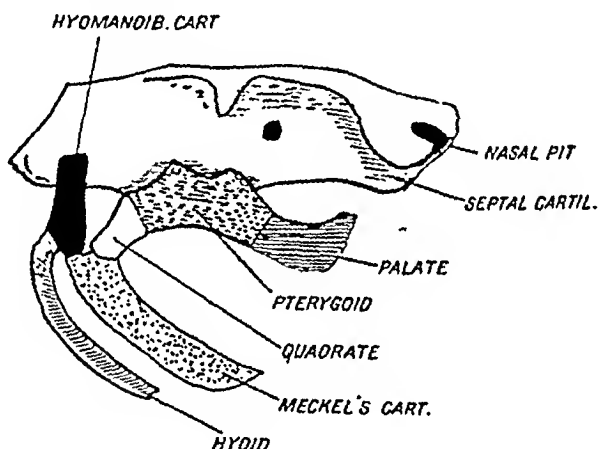


FIG. 208. The Cartilages in the Nasal, Maxillary, Mandibular and Hyoid Processes of a Shark.

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The mandibular process has also a cartilaginous bar developed within

separated from the mouth by the canine and molar tooth sacs. The maxilla rests on the outer aspect of the lateral nasal process, and to some extent assists that process to form the outer wall of the nasal cavity (Fig. 204). In the 3rd month of foetal life the mucous membrane in the middle meatus begins to bud outwards, presses before it and bursts

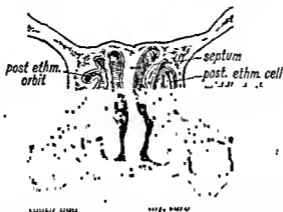


FIG. 210. Coronal section of the Nasal Cavities of a newly born Child, showing the development of the hiatus semilunaris and air sinuses.

through the lateral nasal plate of cartilage and begins to distend the maxillary process. On the growing margin of the bud are processes which appear to be glandular in nature [21]. At birth the sinus is only a shallow recess on the outer wall of the middle meatus, above the germ of the first milk molar (Fig. 210). It continues to grow until the 25th

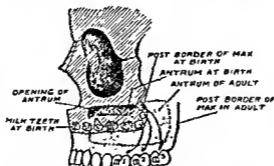


FIG. 211 Showing the manner in which the development of the Maxillary Antrum affects the size of the palate and position of the molar teeth.

year, and is the only one of the air sinuses developed from the nasal cavity which is more than a rudiment at the time of birth. In the years of adolescence the sinus expands until it inflates the maxillary part of the malar (os zygomatici). As it expands backwards the posterior border of the maxilla, which contains the buds of the permanent molar teeth, undergoes a rotation downwards, so that what was situated on the posterior border comes to be situated on the alveolar border (Fig. 211).

the scalp of the foetus during the 3rd month of development. A close network of capillaries spreads upwards in the scalp on each side of the head until the invading networks meet in the mid-line of the crown. Greig has reported cases in which the vascular networks have failed to reach the mid-line, leaving bald cicatricial-looking patches [19].

Formation of Foramina and Canals in Bone.—The development of canals and foramina in the bones of the maxillary process illustrates the manner in which these are formed in the skull generally. Many foramina and canals occur between elements which unite in the course of development (see p. 223). The Vidian nerve lies between the internal pterygoid plate (a separate bone) and the external pterygoid, a plate which is formed in the maxillary process as a prolongation of the great wing of the sphenoid. The pterygo-palatine canal is situated between the pterygoid and palatal parts of the palato-quadrato bar. The descending palatine nerve lies between the palate bone and superior maxilla. These are canals formed between different elements. The infra-orbital nerve at first passes forwards in a groove on the orbital aspect of the superior maxilla, but in the later months of foetal life, upgrowths from the orbital centre of ossification of the maxilla meet over the nerve and convert the groove into a canal.

The foramen rotundum and foramen ovale are at first notches on the edge of the great wing of the sphenoid, but in the course of foetal growth the notches are converted into foramina. Hence wherever a nerve foramen or canal is found one may conclude that it marks the junction of two elements, originally distinct, or that it is originally a groove or notch on the edge of the bone (Bland-Sutton). The foramina for nerves in the malar bone appear to be exceptions to this rule. Only one centre appears for the ossification of this bone (7th week), and the nerves evidently become involved during the ossification of the membranous basis. The malar bone is occasionally ossified from two centres which may fail to unite; the bone is then divided by a suture passing from the orbit to the temporal fossa. A divided malar occurs rather more frequently in Japanese and other Mongolian skulls, hence the name of *Osjaponicum*.

Palatal Rugae [20].—In all orders of mammals the mucous membrane on the hard palate is ridged transversely; three or four of these transverse ridges are seen on each side of the palate of the newly born child; they tend to disappear in the adult. Food is triturated between them and the rough papillae on the palatal aspect of the tongue. Their disappearance in man is probably due to the soft nature of his food.

Maxillary Sinus.—It will be seen from Fig. 210 that the maxilla at birth forms a plate of bone in the floor of the orbit, this plate being

209). The 3rd division of the Vth is its nerve, but its artery, the first aortic arch, has only a transient existence, although the inferior dental may represent part of it.

Development and Ossification of the Lower Jaw [24].—In Fig. 213, which represents the condition of the human mandible at the beginning of the 4th month, the primitive cartilaginous skeleton of the mandibular arch can still be followed from the symphysis to the tympanum. Only one part of the cartilage takes a direct share in the formation of the mandible—that part which lies near the symphysis and assists to form the section of the mandible which carries the first premolar and canine teeth. The ventral extremities persist through foetal life as cartilaginous nodules; they may become ossified [25]. The proximal end of Meckel's cartilage forms the malleus; all the rest of the bar disappears, although the long internal lateral ligament occupies the site of part of the cartilage.

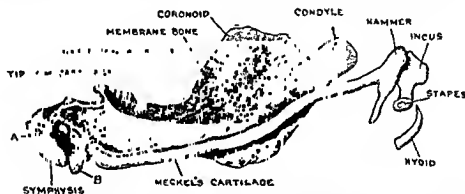


FIG. 213. Meckel's Cartilage and Mandible of a Fœtus in the 4th month of development, viewed on the inner or lingual aspect. (From a drawing and reconstruction by Prof. Alex. Low.) A and B, cartilaginous ossicles at symphysis.

In rare instances the cartilage may undergo complete and independent ossification. Thus the lower jaw, which shares with the clavicle the distinction of being the first bone in the body to ossify, is a membrane or dermal bone. Late in the 7th week a centre of ossification appears in each half, on the outer side of the Meckel's cartilage and near the site of the future mental foramen. Each half of the lower jaw is ossified by the extension of a single centre. Processes grow up on either side of the inferior dental nerve, which, with the tooth buds, comes to lie in a primitive alveolar trough. During the 3rd month the ascending ramus begins to form. In the condylar and coronoid processes a formation of secondary cartilage occurs, fibroblasts being converted into cartilage cells; thus the condyle and coronoid are ultimately laid down in cartilage. The two halves of the mandible unite at the symphysis during the second year; in some animals, such as the kangaroo, the symphysis remains open.

If the processes of growth and rotation are arrested, the last molar (wisdom) tooth is left on the posterior border of the maxilla, where it may give rise to pain and suppuration. The maxillary sinus or antrum is peculiarly large in man and in anthropoid apes. It is small in monkeys, a greatly expanded inferior meatus taking its place [22].

Mandibular Process and Arch.—The two mandibular processes unite in the middle line and form the mandibular or first visceral arch. The arch forms the lower or hinder boundary of the stomodaeum (Fig. 212). The right and left processes are in contact in the 4th week of develop-

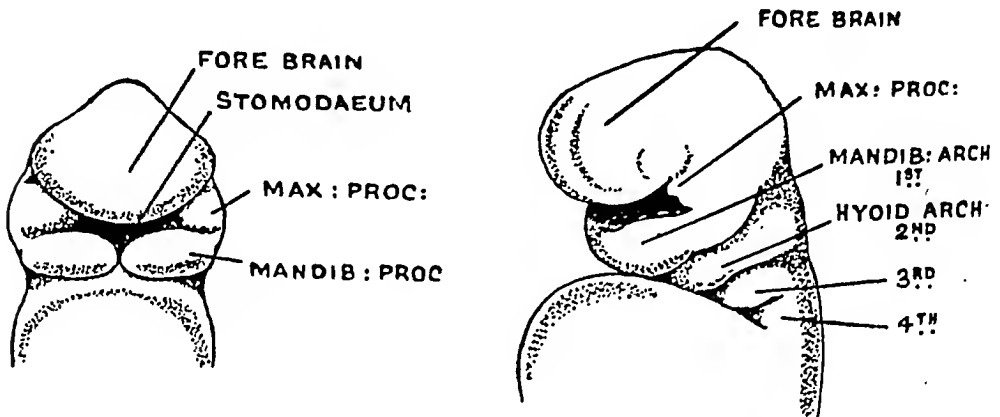


FIG. 212. The Mandibular Arch and Stomodaeum (primitive mouth) in a Human Embryo of the 5th week. (After Rabl.) A, from the front; B, from the side.

ment, but the process of fusion, which may be arrested (Fig. 192), is not complete until the middle of the 2nd month.

Parts formed from the Mandibular Arch.—Besides the lower jaw, there are formed from this arch the soft parts over and under the jaw, the lower lip, the muscles of mastication, the mylo-hyoid and anterior belly of the digastric, the tensor palati, and the tensor tympani. The anterior two-thirds of the tongue, the sublingual and submaxillary glands are formed from the mandibular arch and from the floor of the primitive pharynx between the mandibular and the second or hyoid arch. These parts are supplied from the nerve of the mandibular arch. The whole arch and its derivatives are set apart primarily for the purpose of seizing food, and secondarily for mastication. Only in mammals are the *lips* separated from the alveolar processes. In the human embryo the lower lip is demarcated from the alveolus by the downgrowth of an epithelial groove (the labio-alveolar plate or groove) about the middle of the 7th week. At birth the margin of the lips is covered by a villous zone [23].

The *Mandibular Arch* bounds the stomodaeum behind, and is the foremost of the visceral arches which encircle and form the walls of the primitive pharynx. *Meckel's cartilage* forms its skeletal basis (Figs. 208,

each other accurately in chewing. Growth of the upper jaw and of the antrum of Highmore requires a descent of the body of the lower jaw and an elongation of the ascending ramus (Fig. 214). In old age, when the teeth drop out and the alveolar margins are absorbed, the ascending ramus again becomes oblique, to allow the lower jaw to come in contact with the upper during mastication. The mental eminence is present at birth, and is a human characteristic [27]. In apes the genioglossal muscles arise from a fossa, in place of a tubercle as in man, on the lingual aspect of the symphysis. In primitive races this simian fossa occasionally occurs [28].

Prof. Brash has shown that the bone which forms the alveolar parts of the jaws is laid down in a complicated manner and is particularly plastic in its nature [26]. As the teeth erupt, new bone is formed both at the lower and alveolar borders of the mandible, and also over the mental eminence or chin. These growth changes are well exemplified in the subjects of acromegaly (Fig. 214). In this disease growth of the jaw continues after adult years are reached. The deposition of new bone at the condylar process leads to the chin and teeth being pushed forwards in front of the upper jaw and teeth. The chin and lower border also increase in size [29].

Temporo-mandibular Articulation.—Two types of this joint are found in mammals, one (see Fig. 215, *A*) exemplified in the carnivora, in which only a hinge action is permitted, and hence the jaws act like scissor blades; the second (see Fig. 215, *C*), in which a gliding movement is allowed, the teeth being thus able to act as grinders. The second type occurs in all vegetable feeders. The human articulation combines the characters of both types (Fig. 215, *B*), the gliding action taking place between the interarticular cartilage and the skull, the hinge action between the cartilage and the condyle [30]. In rodents the glenoid cavity is a narrow gutter in which the plate-like condyloid process glides backwards and forwards. The interarticular cartilage is developed in all the Mammalia except the monotremes and one or two marsupials [31]. At the end of the 3rd month the cartilage appears as a condensation of fibrous tissue between the coronoid process and root of the zygoma. There is at this time no articular cavity; the disc appears to arise from tissue caught between the condylar process and future glenoid cavity (Vinogradoff). The joint is lined not by cartilage but by connective tissue [32]. This is a feature which is to be seen in all joints at an early stage of development, but in this case it may be owing to the evolutionary history of the joint (see p. 253).

Development of the Tympanic Plate and Articular Eminence.—If the chin be depressed the condyle of the jaw moves on to the articular

Evolution of the Mandible.—To interpret the appearances seen during the development of the human mandible we must suppose that Meckel's cartilage is the primitive skeleton of the mandible—a condition we know to occur in various forms of fishes (see Fig. 208). The malleus formed the upper end of the skeleton of the jaw, the joint between the malleus and incus representing the mandibular joint. The second stage in the evolution of the jaw is the formation of membrane or dermal bone to strengthen the cartilaginous rod and form supports for the teeth. This stage is also seen in fishes. The third and final stage is the formation of an ascending ramus and the evolution of a new joint between the condyle of the ascending ramus and the squamosal part of the temporal. This stage evidently occurred in the early ancestry of the mammals. Some of the transitional changes have been observed in the mammal-like reptiles of South Africa [18]. In all other vertebrates—amphibians, reptiles and birds—the primitive joint persists.

Growth Changes in the Jaw.—The mandible undergoes great changes

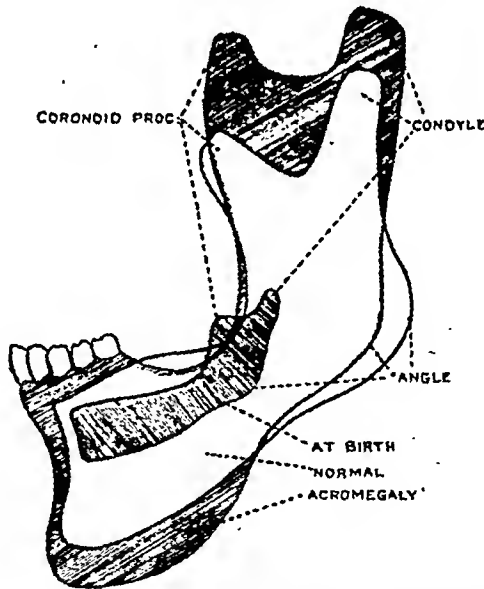


FIG. 214. Mandibles of a Child at Birth, of a Normal Adult and of a Man the subject of Acromegaly, superimposed to show the manner in which growth takes place.

in the course of growth. As the permanent teeth erupt behind the milk set, increased alveolar space is required. This is obtained (see Fig. 214) in two ways, by a forward movement of the teeth and their sockets and by new bone being deposited along the posterior border of the ascending ramus. Growth in the vertical height is obtained by the deposition of new bone along the upper border of the ramus [26]. There must be a growth mechanism for regulating the rates of increase of the upper and lower jaws: otherwise the upper and lower teeth would fail to oppose

easily accessible to the surgeon (Fig. 216, C). The plate also grows inwards to form the floor of the bony part of the Eustachian tube and downwards to form the vaginal process, to which the upper end of the carotid sheath is attached (Fig. 216, C).

Fate of the Stomodaeum.—Having described the manner in which the three developmental masses—nasal, maxillary and mandibular—are involved in the upbuilding of each side of the face, it may be profitable

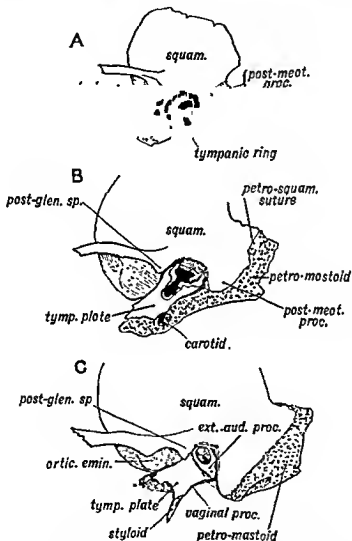


FIG. 216. Showing the chief changes after birth in the form of the Temporo-Maxillary Articulation.

A. At birth. B. At two years. C. In the adult.

to look back and see what has become of the primitive oral cavity—the stomodaeum. A diagrammatic section of this cavity is given in Fig. 217; up to the 5th week it is separated from the primitive pharynx by the oral membrane; the stalk of the pituitary evagination—Rathke's

eminence (Fig. 215, *B*); if over-depressed it springs over the eminence, and a dislocation is produced. This is impossible in the early years of life, for at birth there is no eminence and no glenoid cavity (see Fig. 216, *A*). At birth the *membrana tympani* lies exposed on the surface of the skull behind the condyle, supported in a fine osseous hoop, the *tympanic ring*. The ring is imperfect above, and there the flaccid part of the membrane occurs. By the second year the ring has grown into

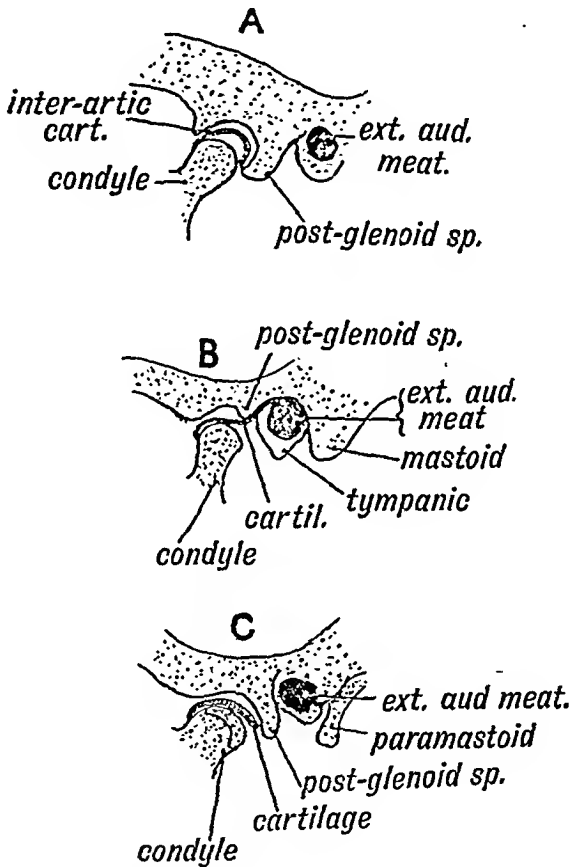


FIG. 215. The chief types of the Temporo-Maxillary Articulation.
A. Carnivorous Type. B. Omnivorous Type. C. Herbivorous Type.

a plate by sending out two processes, which, as they grow out, unite and leave a gap between (Fig. 216, *B*). This, as a rule, is filled up by the 4th year. By the 20th year the tympanic plate is three-quarters of an inch long, forming the bony floor of the external meatus and the posterior wall of the glenoid fossa, which in man is remarkably deep. It protects the meatus from the condyle, and must be regarded as an accessory part of the mandibular joint. Every year until the 20th the bony meatus grows longer, while the fibro-cartilaginous part becomes relatively shorter. In the adult the bony part forms two-thirds of the meatus. As the tympanic plate grows outwards, the *membrana* becomes less

but only part of the soft. The nasal cavities are not derived from the stomodaeum. It is true that the nasal processes grow within and fill up the primitive space as it expands, but the cavities within the nasal processes represent expansions of the primary olfactory pockets. The tongue and floor of the mouth arise in the pharynx, behind the oral plate.

In this chapter an account has been given of the various embryological elements which go to form the face. In the chapters dealing with the eye, nose, teeth and tongue further details will be described. The chief feature of the human face is its power of expression—due to the high differentiation of its subcutaneous musculature and to the elaborate nervous mechanism controlling that musculature [33]. The muscles of expression, we shall see, arise in connection with the hyoid arch; their wide distribution on the face occurred with the evolution of the pulmonary respiratory system.

NOTES AND REFERENCES

[1] For the evolution of the face, see Gregory, W. K., *The Evolution of the Face from Fish to Man*, 1929; Wood-Jones, F., *Man's Place amongst the Mammals*, 1929. For an account of development of the face, see Prof. Frazer's *Manual of Embryology*, 1940, Chapter XV.

[2] In the present edition I have given up the teaching of Prof. His, the founder of Human Embryology, namely that the middle part of the upper lip is formed by the mesial nasal processes, and adopted that of Prof. J. E. Frazer, who found that the upper lip, almost in its entirety, is formed by the meeting of the maxillary processes. See also Boyd, J. D., *Jour. Anat.*, 1933, 67, 439; Barge, J. A. J., *Zeitsch. Anat. Entwickl.*, 1936, 105, 264.

[3] For a comparison of the union of embryonic parts with the healing of wounds,

1900, 103, th, Sir A., *Brit. Med. Jour.*, 1909, 1, 310; *Brit. Jour. Surg.*, 1910, 28, 173. For hereditary nature of hare-lip, see Hogben, L., *Jour. Genetics*, 1932, 25, 211, 293; Schroeder, C. H., *Archiv. Rass. Ges. Biol.*, 1931, 25, 369.

[4] For report of cases, see Derry, D. E., *Jour. Anat.*, 1938, 72, 294; Reese, A. M., *Anat. Anz.*, 1937, 84, 193.

[5] For experimental production of Cyclops, see Job, Leibold and Fitzmaurice, *Amer. Jour. Anat.*, 1935, 56, 97 (rat embryos exposed to dosage of X-rays); Wolff, E., *Archiv d'Anat.*, 1934, 18, 147, 231 (chick embryos exposed to radiations); see also notes [10], [25], Chapter IV.

[6] *Jour. Anat.*, 1906, 40, 400; see summary of Prof. Fawcett's observations on ossification of the face, *Publications of the Dental Board*, 1928; see also reference to Prof. Frazer under preceding note [1]; Broman, I., *Die Entwicklung des Menschen*, 1927, p. 270; Augier, M., *C.R. Ass. d'anat.*, 1932, p. 18 (ossification of the premaxilla).

pocket—is connected with the stomodaeum at the dorsal margin of the membrane. When the prechordal or trabecular plate of cartilage is formed below the fore-brain, the *pituitary body* thus becoming an intra-

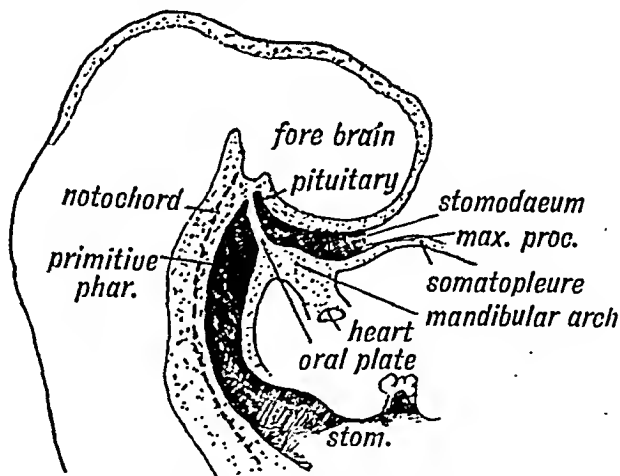


FIG. 217. Sagittal section showing the Stomodaeum and position of the Oral Plate in the 4th week. (Schematic.)

cranial organ, its stalk comes to be situated at the hinder or sphenoid end of the nasal septum or vomer. This vomerine point may be regarded as stationary during the development of the nasal and buccal

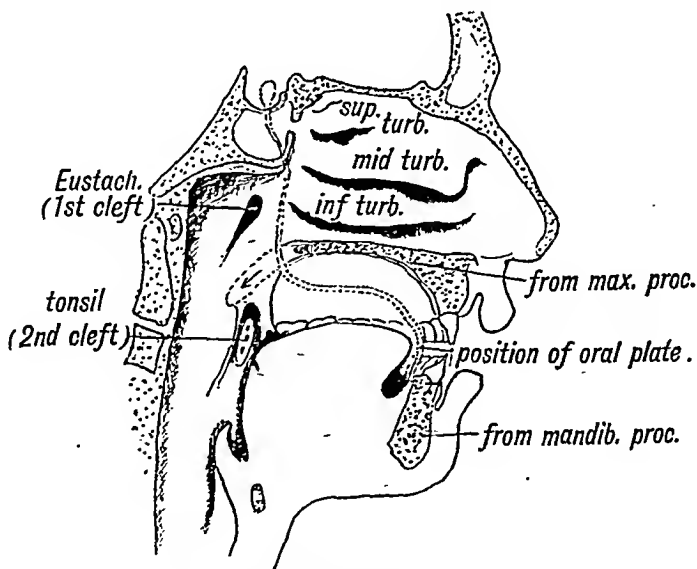


FIG. 218. Showing the fate of the Stomodaeum. The relative position of the oral plate is indicated.

cavities. In Fig. 218 there is shown the position and relationships which the oral plate would assume were it to persist until adult life. The lips and teeth are developed in front of it, and therefore within the cavity of the stomadaeum. The hard palate is developed in front of it,

in Children," *Rep. Med. Resear. Coun.*, 1932, No. 171; Todd, T. W., *Internat. Jour. Orthodont.*, 1932, 18, 799; Hellman, M., *ibid.*, 1932, 18, 777; 1933, 19, 1116; Goldstein, M. S., *Amer. Jour. Phys. Anthropol.*, 1937, 22, 37.

[27] Hrdlicka, A., *Amer. Jour. Phys. Anthropol.*, 1930, 14, 317; Weidenreich, F., *Ergeb. Anat. Entwickl.*, 1934, 31, 1; McCown and Keith, *Men of the Old Stone Age of Mount Carmel*, 1939.

[28] Thomson, Arthur, *Jour. Anat.*, 1916, 50, 43; Keith, Sir A., *Antiquity of Man*, 1925; McCown and Keith, see under preceding note.

[29] Keith, Sir A., *Lancet*, 1911, 1, 993, 1002 (acromegaly).

[30] Wustrow, P., *Ergeb. Anat. Entwickl.*, 1938, 32, 137 (movements of mandible).

[31] Parsons, F. G., *Jour. Anat.*, 1900, 34, 41.

[32] Charles, S. W., *Brit. Dental Jour.*, 1925, 46, 845.

[33] Huber, E., *The Evolution of Facial Musculature*, 1931.

[7] Burkitt and Lightoller, *Jour. Anat.*, 1923, 57, 295; Johnson, E. H., *ibid.*, 1937, 71, 356.

[8] Prof. Wood-Jones's account of the submergence of the human premaxilla by an overgrowth of the maxilla will be found in the *Jour. Anat.*, 1938, 72, 462. See also his *Man's Place amongst the Mammals*, 1929, and E. H. Johnson's account in the *Jour. Anat.*, 1937, 71, 356. Prof. Wood-Jones found that G. W. Callender, a London surgeon, had anticipated him in 1870 (*Phil. Trans.*, 1870, 159, 163). Prof. Ashley-Montagu also rediscovered Callender's account of a maxillary invasion of the premaxillary region and re-introduced the conception (*Quart. Jour. Biol.*, 1935, 10, 32, 181; *Jour. Amer. Dent. Ass.*, 1936, 23, 2043). What Callender really discovered was that the greater part of the human premaxilla is developed from the maxillary process, mistaking it for an overgrowth from the maxilla. The first man to give a clear exposition that the mammalian premaxilla arises from two embryonic elements, mesial nasal and maxillary, was Dr. D. Biondi in *Virchow's Archiv.*, 1888, 111, 125. It is Biondi's account that is followed in my text. For other papers on the dual origin of the premaxilla, see Norberg, O., *Zeitsch. Anat. Entwickl.*, 1933, 100, 394; Franz, V., *Ergeb. Anat. Entwickl.*, 1933, 30, 469.

[9] See *Jour. Anat.*, 1939, 73, 583.

[10] Derry, D. E., see under note [4].

[11] Ashley Montagu, M. F., *Amer. Jour. Phys. Anthropol.*, 1942, 29, 417 (photograph of the premaxillary region of a gorilla's skull in which the suture between the lateral and mesial elements of the premaxilla persists on the facial aspect).

[12] See Broman, I., reference in note [6]. Minnett, F. C., *Jour. Anat.*, 1925, 60, 110. See also references given in note [8], p. 294.

[13] For details of formation of nasal duct, see Frazer, J. E., reference in note [1].

[14] For spread of mesoderm of the maxillary process, see p. 238. Also Prof. Frazer's account: reference in note [1]. Prof. Lockhart has reported (*Jour. Anat.*, 1929, 63, 234) a case of arrest of development of both mandibular and maxillary processes.

[15] Pons-Tortella, E., *Anat. Anz.*, 1937, 84, 13.

[16] Frazer, J. E., *Jour. Anat.*, 1911, 45, 190.

[17] Edgeworth, F., *Jour. Anat.*, 1930, 64, 184; Frazer, J. E., see under note [1]; Lightoller, G. H. S., *Trans. Zool. Soc. Lond.*, 1939, 24, 349.

[18] Broom, R., *The Mammal-like Reptiles of South Africa*, 1932.

[19] Finley, E. B., *Contrib. Emb.*, 1922, p. 155; Greig, D., *Edin. Med. Jour.*, 1931, 38, 341.

[20] West, C., *Contrib. Emb.*, 1925, 16, 25.

[21] Broman, I., see under note [6].

[22] Keith, Sir A., *Proc. Anat. Soc.*, May, 1902; *Brit. Jour. Dent. Sc.*, 1902, 45, 529; Schaeffer, J. P., *Amer. Jour. Anat.*, 1912, 13, 1; Wood-Jones, F., *Jour. Anat.*, 1939, 73, 116 (maxillary sinus of gorilla); Cave and Haines, *ibid.*, 1940, 74, 493 (nasal sinus as in anthropoids).

[23] Wherry and Anson, *Amer. Jour. Anat.*, 1936, 58, 73.

[24] Fawcett, E., *Jour. Anat.*, 1930, 64, 369; Low, A., *ibid.*, 1910, 44, 83; Keith, Sir A., *ibid.*, 1910, 44, 151 (abnormal ossification of mandibular arch).

[25] Smith, Sydney, *Jour. Anat.*, 1925, 59, 388.

[26] Brash, J. C., "The Growth of the Jaws, Normal and Abnormal," *Publications of the Dental Board*, 1926; "Etiology of Irregularity and Malocclusion," *ibid.*, 1931; Campion and Keith, *Dent. Rec.*, 1922, 42, 61; Young and Smyth, "Facial Growth

part or crown of the dentine is coated by (iii) the *enamel*; the embedded part or root by a layer of bone—(iv) the *crusta petrosa*. The root is secured within its socket by (v) the *peridental membrane*, which acts as a periosteum to both the (vi) *crusta petrosa* and bony wall of the tooth socket. An account of the development of a tooth has to deal with the origin of each of these parts.

(i) *Origin of the Enamel*.—The enamel buds are formed by the ectoderm of the stomodaeum. In the 7th week the ectoderm within the labial margin grows into [5] the underlying mesodermal tissues so that a narrow semicircular invagination of epithelium is formed within the mandibular arch below, and within the premaxillary and maxillary parts of the primitive palato above. To the plate of ectoderm thus infolded the name of *dental lamina* or *shelf* is given. As may be seen in a section

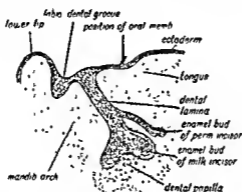


FIG. 222 Section through the Lip and Mandible of a Foetus in the 3rd month of development, showing the down-growth of the dental shelf.

of the foetal lower jaw (Figs. 220, 222) the dental lamina is continuous at its origin with the epithelial downgrowth which separates the lip from the alveolus. From the ingrowing or deep margin of the dental lamina ten epithelial buds arise during the 3rd month, both in the upper and lower jaw. Each of these twenty *enamel buds* or *organs* produces the enamel to cover the crown of a milk tooth. Each bud as it deepens and expands comes against a condensed formation in the mesoderm of the jaw—the *dental papilla*. On the papilla the enamel bud becomes partly invaginated, the mesodermal or odontoblastic bud coming to lie within the invagination (Fig. 222). During the 4th month the deeper stratum of ectodermal cells which cover the papilla change into columnar enamel-producing cells or *ameloblasts* [6]. The basal part of the ameloblasts is converted gradually into enamel, or to put it somewhat differently, the ameloblasts form and deposit enamel at their bases and thus produce a coating for the dental papilla (Fig. 223). Each ameloblast thus gives rise at its base to a minute hexagonal prism of enamel.

lamina. The buccal epithelium which forms the labial and dental lamina is usually described as growing down into and invading the underlying mesoderm. Prof. J. E. Frazer [3] has given proof that it is the opposite that is true; the mesoderm grows up and isolates dental and labial lamina, the superficial parts of both being fused in the labio-dental lamina. The inner aspect of the lips is also covered by a carpet of villi at birth, very similar to that on the gums [4].

Evolution of Teeth.—The teeth are products of the skin. Both the cutis or dermis and the epithelium or epidermis enter into their formation. A tooth is a papilla of the dermis which has undergone a peculiar form of ossification (dentine); it is coated by an extremely hard substance,

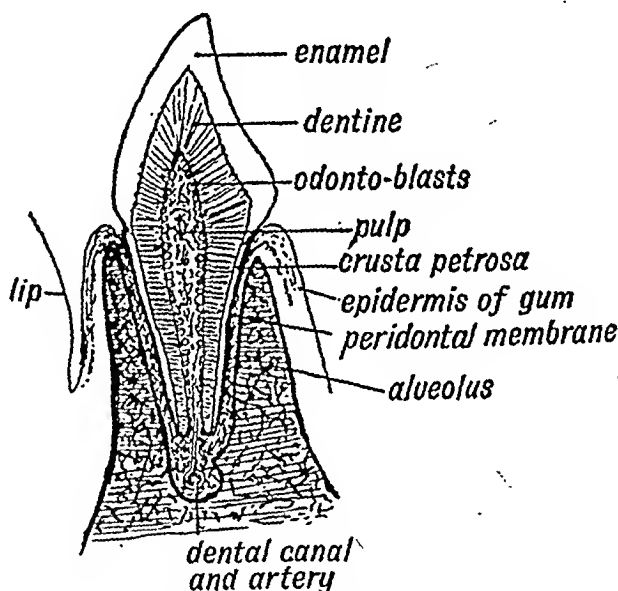


FIG. 221. Showing the parts of an Incisor Tooth.

enamel, which is formed by the epidermis. Between the placoid scales which cover the skin of a shark and the complicated molar tooth of an elephant there is a connecting series of intermediate forms. The primitive teeth have a conical or peg-like form, but with the evolution of mastication in the primitive mammalian stock the conical teeth became differentiated into various and complicated forms—the molar teeth departing very markedly from the primitive simple type. The recognition of the true nature of teeth was delayed by the fact that during development the dental papilla and its epidermal covering are submerged beneath the lining membrane of the mouth.

Structure of a Tooth.—A tooth may be considered as made up of six parts (see Fig. 221):

- (i) The *pulp*, situated within (ii) a capsule of *dentine*; the exposed

tooth. Fine processes of the nerves pass into the dental tubules, while in its peripheral zone are situated cells possessing the characteristics of nerve cells [11].

(iv) *Dental Sac*.—Each foetal tooth, as may be seen from Fig. 224, lies embedded in the alveolus surrounded by a fibrous capsule known as the dental sac. The sac and its contents form a *dental follicle*. When the enamel bud is invaginated by the dental papilla, the *invaginated* wall forms the enamel-producing layer, while the *invaginating* or parietal wall becomes surrounded by a dense layer of mesodermal tissue. The parietal wall is converted into the dental sac. At first (Fig. 224) the dental sac is continuous with the pulp papilla; it becomes separated from the pulp when the root or roots of the teeth are completed. Between the enamel

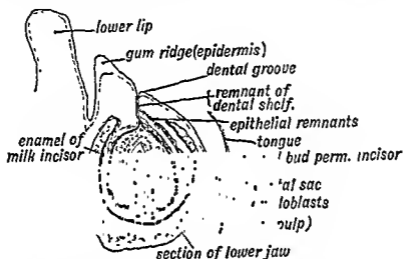


FIG. 224 Showing the stage of development in an Incisor Tooth of a Foetus of 6 months.

(invaginated) and parietal (invaginating) layers, filling the cavity of the sac, lies a mass of jelly-like epithelium corresponding to the corneous epithelium of the skin. As the crown of the tooth grows it rises within the sac of the enamel germ, and causes the absorption of the gelatinous material (Fig. 225).

(v) *Peridental Membrane*.—The peridental membrane (Fig. 221) is formed by that part of the dental sac which surrounds the fang of the tooth. It becomes the periosteal ligament which binds the root to its socket; it is furnished with special nerve endings [11]. The part of the dental sac which surrounds the crown is absorbed during the eruption of the tooth.

(vi) *Crusta Petrosa*.—The peridental membrane is of the nature of periosteum, and contains osteoblasts which deposit the crusta petrosa (bone) on that part of the dentine which forms the fang and also on the

When the prisms are completed the ameloblasts form a *cuticular membrane* (Nasmyth's membrane) which covers the enamel at birth and is soon afterwards worn off. The enamel of the milk teeth begins to be laid down late in the 3rd month and is completely formed before birth; and that of the first permanent molar begins to be deposited at birth or soon after [7]. From the 5th month onwards the dental lamina—between the tooth germs and the surface of the alveolar margin—undergoes a gradual disruption and absorption. Isolated masses of the lamina may persist within the gums and in certain cases give rise to masses of dental tissue—odontomes [8].

(ii) *Origin of the Dentine.*—The dental papilla or odontoblastic germ,

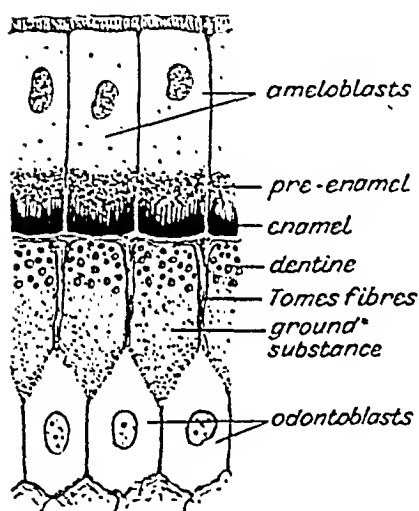


FIG. 223. Diagram to show the manner in which enamel is laid down by ameloblasts and dentine by odontoblasts. The main process of an odontoblast (Tomes' fibre) ends in the fine reticular membrane which separates the formed enamel from the formed dentine.

formed from the mesoderm, corresponds to a depressed skin (dermal) papilla, the enamel cells representing its covering of epithelium. The dental papilla determines the shape of the tooth. In its superficial layers it contains numerous cells, *odontoblasts*, with processes radiating towards the enamel epithelium (Fig. 223). By the agency of the odontoblasts a substance is deposited which becomes calcified into dentine or ivory [9]. It is deposited in the matrix round the processes of the odontoblasts. The cavities in which the processes are enclosed become the tubules of the dentine. In rodents especially, but also in all mammals, although only to a slight extent in civilized races of

mankind, the odontoblasts react to wear, add new layers of dentine to the wall of the pulp cavity, and thus prevent the pulp from being exposed. The dentine is deposited first in the crown of the tooth beneath the enamel; the neck is laid down next, and then the root, the last point of all to be formed being the narrow canal at the apex of the root by which the dental vessels and nerves reach the pulp cavity. The dental crowns reach their full size at the time of their formation. Teeth thus differ from all other structures of the body in undergoing no growth subsequent to the period of their development [10].

(iii) *The Pulp.*—The pulp represents the remnant of the odontoblastic germ enclosed by the dentine. It is made up of a matrix of branching cells and contains the ramifications of the artery, vein and nerve of the

tooth. Fine processes of the nerves pass into the dental tubules, while in its peripheral zone are situated cells possessing the characteristics of nerve cells [11].

(iv) *Dental Sac*.—Each foetal tooth, as may be seen from Fig. 224, lies embedded in the alveolus surrounded by a fibrous capsule known as the dental sac. The sac and its contents form a *dental follicle*. When the enamel bud is invaginated by the dental papilla, the *invaginated* wall forms the enamel-producing layer, while the *invaginating* or parietal wall becomes surrounded by a dense layer of mesodermal tissue. The parietal wall is converted into the dental sac. At first (Fig. 224) the dental sac is continuous with the pulp papilla; it becomes separated from the pulp when the root or roots of the teeth are completed. Between the enamel

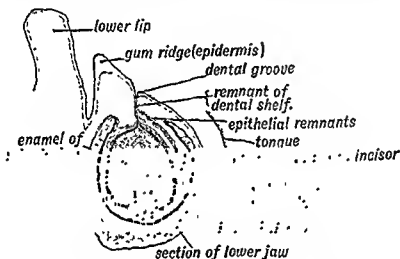


FIG. 224. Showing the stage of development in an Incisor Tooth of a Foetus of 6 months.

the cavity of the
to the corneous
epithelium of the skin. As the crown of the tooth grows it rises within the sac of the enamel germ, and causes the absorption of the gelatinous material (Fig. 225).

(v) *Peridental Membrane*.—The peridental membrane (Fig. 221) is formed by that part of the dental sac which surrounds the fang of the tooth. It becomes the periosteal ligament which binds the root to its socket; it is furnished with special nerve endings [11]. The part of the dental sac which surrounds the crown is absorbed during the eruption of the tooth.

(vi) *Crusta Petrosa*.—The peridental membrane is of the nature of periosteum, and contains osteoblasts which deposit the crusta petrosa (bone) on that part of the dentine which forms the fang and also on the

inner wall of the alveolus. The centres of ossification in the upper and lower jaw spread round the labial and lingual aspects of the dental sacs, thus enclosing them in a bony gutter or trough. Subsequently septa are developed between the dental sacs, and thus the developing teeth come to be situated in bony crypts. The roof of a crypt is never completed; a hole or window persists through which the neck of the dental sac emerges to become continuous with the mucous membrane covering the alveolus. The crowns of the teeth erupt at the point of union between the dental sac and alveolar membrane.

Epithelial Remnants of Enamel Organ.—Epithelial remnants of the dental lamina are to be found in the substance of the alveolus up to the

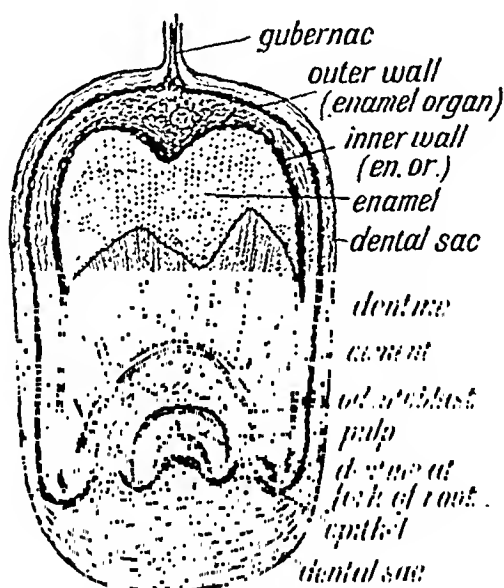


FIG. 225. Epithelial remnants in the Dental Sac of a 1st Permanent Human Molar. (Howard Mummery.)

end of foetal life or later, and may give rise to cysts of various kinds [8]. Besides these there are also others which occur within the sac surrounding an uncut tooth, representing remains of the enamel organ. In Fig. 225 is depicted a section of an unerupted first permanent molar tooth, lying within its dental sac, remnants of the enamel organ being shown distributed within the sac from the crown to the growing ends of the roots. We have seen that the enamel organ represents an epithelial sac, only the inner or invaginated wall being concerned in the formation of the enamel, the outer or enveloping layer becoming broken up as shown in Mr. Mummery's figure, to form an interrupted epithelial layer sometimes named Hertwig's sheath [12].

Origin of the Permanent Teeth.—From the dental shelf, besides the buds for the milk teeth, there grow inwards, during the latter part of

the 3rd month of development, so as to lie on the lingual aspect of the milk buds, processes of ectoderm which form the enamel of the ten teeth which replace the milk teeth (Figs. 222, 224 and 227). The three permanent molars of each side arise from a process which prolongs the dental lamina backwards behind the part from which the enamel buds of the milk teeth arise (Fig. 227). The first molar is the earliest of all the permanent teeth to undergo development. The permanent teeth are formed in exactly the same manner as the milk set. They develop on the lingual aspect of the roots of the milk teeth, and if the milk teeth be roughly extracted the permanent bud may also be torn out. Being

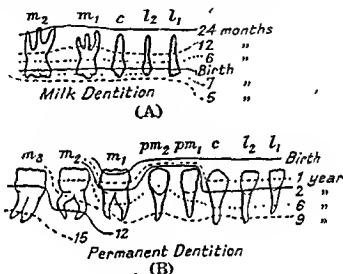


FIG. 220

B. Diagram to show the dates at which the various parts of the Permanent Teeth are formed. (Dr. Lawson Dick.)

developed deeper in the alveolus than the milk teeth, the neck of the dental sac is more elongated, and has been named the *gubernaculum dentis* under the belief that it serves to guide the teeth during eruption. The opening by which the gubernaculum emerges from the crypts of the permanent incisors and canines is seen on the lingual side of the alveolus near the sockets of the corresponding milk teeth. In the case of the premolars, the openings lie within the crypts of the milk molars (Carter).

Dates of Formation.—It is important from a clinician's point of view to remember when the crowns of teeth are formed, for if during the deposition of enamel and dentine, illness should occur, then an interruption in the process takes place, and when the teeth erupt, their crowns are seen to be marked. In Fig. 226, A, is reproduced a diagram to show when

the milk teeth are formed. The tips of the crowns commence early in the 4th month, and are one-third complete at birth [13]. The only permanent tooth which may begin to form before birth is the 1st molar; usually it begins just after birth. Fig. 226, *B*, shows the dates at which the various parts of the permanent teeth are laid down. The quality of dentine and enamel depend on several factors, some of which are hereditary; of especial importance is the presence in the maternal and foetal blood of a sufficiency of vitamins and inorganic salts [14].

Dentigerous and other Cysts of the Jaw.—Cysts with epithelial walls, containing fluid, teeth or other dermal contents, occasionally develop in the jaw. They are formed from epithelial remnants of the dental lamina,

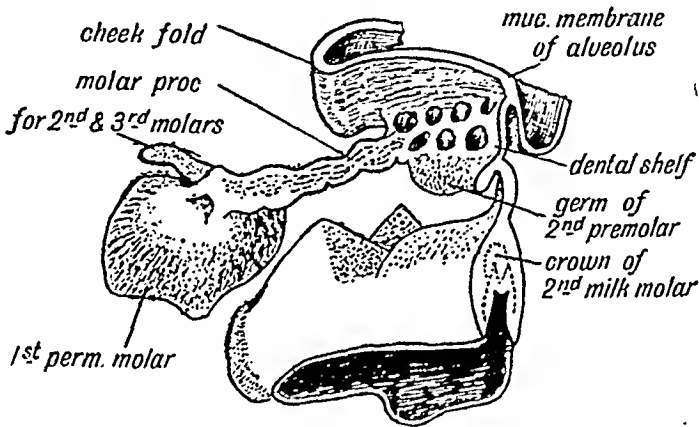


FIG. 227. Mucous Membrane covering the posterior part of the Alveolus of a Newly born Child with the Dental Shelf still attached to it. Proceeding backwards from the end of the dental shelf is seen the "molar process" which gives rise to the three permanent molar teeth. The crown of the second milk molar and the germ of the second premolar are also shown. (After Röse.)

which normally breaks up and disappears completely, or from detached parts of the enamel buds [8].

Number of Dentitions.—In many lower vertebrates, such as sharks, the dental lamina gives off constantly a series of buds, so that as soon as one tooth is lost another springs up in its place from behind (Fig. 228). In mammals generally, as in man, the dental lamina gives off only two series of buds—one for the milk set and another for the permanent set. In marsupials it gives off only one series, so that the first set of teeth is never replaced by a second. Thus in the most primitive vertebrates there is a succession of teeth, owing to the fecundity of the dental shelf. In man there are only the primary and secondary broods, but it is possible that occasionally representatives of a 3rd brood may be produced, for there are cases on record where a permanent tooth has been replaced by another late in life.

Morphology of Human Teeth [15].—The crowns of human teeth seem to be modifications of a single type, all being evolved from the simple

conical tooth found in fishes and reptiles (Figs. 229, 230). The conical peg-like tooth (haplodont) is to be regarded as the most primitive type, and in man vestigial teeth of this type occasionally occur. A modified example of the type is seen in the premolars of carnivorous mammals (Fig. 229). Here the base of the peg-shaped crown is surrounded by a ring of enamel—the *cingulum*. From the conical tooth was evolved the

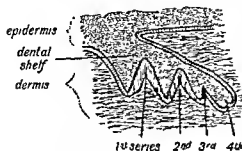


FIG. 228.

FIG. 228. Diagrammatic section across Dental Shelf of a Shark showing a Succession of Dentitions (After Vialleton)

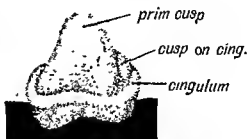


FIG. 229.

FIG. 229. Premolar Tooth of a Carnivorous Mammal to show the Primitive Cone, Cingulum and Secondary Cusps springing from the Cingulum. (Marett Tims.)

tritubercular type, one in which the crown carries three tubercles or cusps, two on the labial side of the crown and one on the lingual margin (Fig. 230, A). Secondary cusps arise from the cingulum (Marett Tims), and by the fusion of these with the original cone two outer cusps are produced, while an inner cusp arises within the cingulum. The canine retains the conical form of crown; the prominence or heel on the lingual aspect

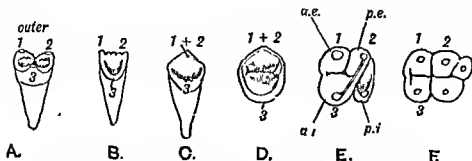


FIG. 230. A. The Tritubercular Type of Tooth. The corresponding cusps are shown in the crowns of an Incisor (B), Canine (C), Bicuspid (D), Upper Molar (E), and a Lower Molar (F).

of the crown represents an inner cusp; occasionally this cusp is well developed on the human canine, particularly in the canine teeth of the extinct Neanderthal race [16]. The cutting edge of the incisors represents the two outer cusps; when newly erupted, the incisor crowns show five serrations or cuspules. In the premolars or bicuspid the outer cusp, as may be seen in many of the lower primates, is really double.

In the upper molar teeth, to the three primary cusps which form a cup, a fourth has been added (see Fig. 230, *E*). The two outer or buccal cusps are distinguished as the A.E. cusp (antero-external), the P.E. cusp (postero-external); the two inner as the A.I. (antero-internal) and P.I. (postero-internal) [17]. In the upper molars the cusps are situated alternately and the P.E. and A.I. cusps are united by an oblique enamel ridge, which represents the posterior margin of the crown of the primitive tritubercular tooth (Fig. 230, *E*). In the upper molar teeth of civilized races, especially in their wisdom teeth, the 4th or posterior internal cusp is often absent, the primitive tritubercular tooth thus reappearing. In the lower molars two cusps have been added to the three primary ones, making five in all. The 5th cusp is situated at the posterior border of the crown; the others are arranged in opposite pairs. The 5th cusp is usually missing from the 2nd and 3rd lower molars of civilized races. The late Prof. L. Bolk collected much embryological evidence in favour of his theory that mammalian teeth had arisen by a fusion or concrescence of dentitions. These dentitions were separate in the reptilian ancestors of mammals [18]. *Gemination* may occur in human incisors; the incisor bud divides so that two crowns are produced on one root [19].

The Roots.—The upper molar teeth have three roots, two outer and one inner, but in the wisdom teeth, especially of civilized races, the roots are usually fused. The lower molars have two roots, but each root appears to be essentially double in nature. In lower primates the upper bicuspid has three roots, but in man these are usually fused so as to form one or sometimes two roots. The lower bicuspid has usually one root, but as in lower apes, they may have two. The roots are the last parts to be formed. When the roots of the molar teeth are being developed, the base of the dental papilla becomes differentiated into three parts—round each of which a root is formed (Fig. 225). In that peculiar ancient and extinct race of men known as the Neanderthal race, the dental papilla and pulp cavity were very large and the roots were short and wide. Thus in *Neanderthal teeth*—the condition is very rarely seen in modern teeth—the pulp cavity almost descended to the tips of the roots. Such teeth are known as “taurodont”—in opposition to the “cynodont” type in which the pulp cavity is small and roots long [20].

Eruption of the Teeth.—The eruption of the milk teeth commonly covers a period of 18 months, beginning in the 6th with the lower incisors and ending in the 24th or 30th with the 2nd milk molars [21]. The eruption of the permanent teeth occupies a period of about 18 years, beginning with the 1st permanent molar in the 7th year and ending about the 24th with the 3rd molar. The milk molars are replaced by

the permanent premolars. In civilized races the 3rd molars or wisdom teeth frequently remain embedded in the alveolus or may be quite absent [22]. The upper wisdom tooth is developed in the posterior border of the superior maxilla, which bounds the spheno-maxillary fissure in front. During the growth backwards of the maxillary antrum the posterior border of the superior maxilla becomes rotated into the alveolar border, thus bringing the wisdom teeth into position (see Fig. 211). The inferior wisdom teeth are developed in the alveolus on the inner aspect of the ascending ramus.

A fourth molar sometimes appears behind the 3rd. The original

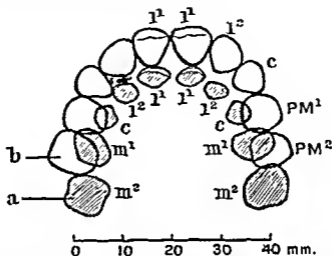


FIG. 231. Showing the forward and outward movement which occurs in the Alveolar Bone of the Jaw as the Milk Teeth are replaced by their Permanent successors. The teeth of the milk dentition are shaded; their successors are unshaded (Prof J. C. Brash)

primate stock is supposed to have had three incisors and four premolars on each side, yet a supernumerary incisor or premolar is a rare abnormality. The upper lateral incisor may be very small or even absent [22], there being a distinct tendency towards the disappearance of this tooth in civilized races. If the teeth are too large for the jaw, a not uncommon condition in civilized races owing to a diminished growth of the bony palate, they appear in irregular positions.

The plastic nature of the alveolar bone is represented by the growth movements which take place as the milk teeth are replaced. There is a complex movement which carries the sockets of the incisor, canine and premolar teeth in the direction shown in Fig. 231. The extent of the movement there represented is a minimal one (Brash).

Mechanism of Eruption [21].—As regards the mechanism which causes teeth to erupt there is still some degree of uncertainty. One naturally infers that the growth of the root will tend to force the crown upwards

and the tissues over the crown to atrophy. The process of eruption is a much more complex one than the mere formation of a root. It is well known that a rootless tooth may cut the gum, while in another case the root may form and yet the tooth remain embedded in the jaw. Eruption is a definite growth movement—allied in nature to the mechanism which leads to the extrusion of a foreign body by the tissues. During the eruption of a tooth there is not only an absorption of the overlying tissues of the gum—probably due to pressure—but there is also the positive growth of the peridontal tissues at the base of the tooth-sac, which, as it presses the tooth towards the surface, moulds the surrounding wall of the dental crypt into a suitable alveolar socket. Thus the formation of the socket or alveolus appears to be part of the mechanism of eruption. All the permanent teeth, but particularly the molars, are moved forwards during and after eruption. The movement is produced by alveolar bone—the most plastic bone of the body.

Effect of Civilization.—Mention has been made of the fact that the eruption of the last molars in highly civilized peoples may be long delayed or arrested; in a proportion of individuals (15%) the germs of two or more of these teeth may be quite absent. When the teeth and jaws of ancient European races are compared with those of their successors, certain changes are very evident. These are: (i) the crowns of the teeth in the ancient races are much worn; (ii) the palate is well formed, and large enough to carry the teeth without crowding or irregularity; (iii) the wisdom teeth are present in a high proportion of individuals, but usually show a reduction in size and development; (iv) diseased and carious teeth are uncommon; (v) the edges of the incisor teeth come into apposition in biting. In modern Europeans the degree of wear or erosion is slight; the palate is often vaulted, contracted and the teeth crowded and misplaced; the wisdom teeth are often unerupted or absent; diseased teeth are extremely common; the edges of the lower incisors ascend behind the crowns of the upper (scissors bite) [23]. The cause or causes of these remarkable changes are ill-understood, but it is probable that some or all will be traced to the nature of our modern dietary [24].

Muscles of Mastication.—The four muscles of mastication—the temporal masseter, external and internal pterygoids arise from the visceral mesoderm of the mandibular arch [25]. A single muscular mass is apparent at the end of the 1st month; during the 2nd month it is differentiated into its several parts—the internal pterygoid being the first to separate from the common mass. The masseter and external pterygoids are derived from the primitive temporal muscle. The external pterygoid is a late addition; even in man it is often imperfectly

separated from the temporal. The muscles of mastication differ from the ordinary striated muscles of the body in being derived from the musculature of a visceral arch. Their motor nerve—the motor root of the Vth—represents the splanchnic nerve of the mandibular segment of the head (see p. 153). The somatic motor nerve of the segment is the IVth or trochlear nerve; the somatic musculature of this segment is represented by the superior oblique. The sensory nerves of the teeth—the 2nd and 3rd divisions of the Vth nerve—represent the skin or somatic sensory fibres of the mandibular segment of the head [26]. It will be thus seen that the apparatus of mastication has been evolved in connection with the 2nd cephalic segment. The manner in which the muscles of mastication are attached to the skull and the extent to which they modify cranial characters have been already mentioned (p. 229). The evolution of the temporo-mandibular joint has also been alluded to (p. 258).

A point in connection with the external pterygoid muscle deserves mention. It is an adductor of the mandible in lower vertebrates, being attached to the upper segment of the mandible which is represented by the malleus in the mammalian head. Harpman and Woollard found, in the human foetus of the 3rd month, that part of the tendon of the external pterygoid extends to the malleus. This connection disappears later, but part of the tendon remains continuous with the meniscus of the temporo-mandibular meniscus [27].

In the Strangeways Laboratory, Cambridge, enamel germs of foetal rats and of other mammals have been transplanted and kept alive in cultural media. They differentiated into enamel and dentine and gave rise to crowns of normal form and structure. If a molar bud was divided, each half gave rise to a complete molar of small size. Dr. Fell found that the ameloblasts are the dominant constituent of a tooth germ; it is they that "evoke" the odontoblasts and determine the shape of the dental papilla [28].

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- [1] West, C., *Contrib. Emb.*, 1925, 16, 25.
- [2] Anson, B. J., *Jour. Morph. Physiol.*, 1929, 43, 335.
- [3] Frazer, J. E., *Manual of Embryology*, 1940.
- [4] Wherry and Anson, see note [3], Chapter XIII.
- [5] While I recognize that Prof. Frazer is right in attributing the formation of the dental and labial laminae as much, or more, to the uprising of the mesoderm as to the ingrowing of the ectoderm, I find it difficult to abandon our older phraseology.
- [6] Mummery, J. H., *The Microscopic Anatomy of the Teeth*, 1920. For development and structure of teeth, see Beams and King, *Anat. Rec.*, 1933, 57, 29;

De Rényi, G. S., *Amer. Jour. Anat.*, 1933, 53, 418 (enamel formation); Karlstroem, S., *Studies of Dental Enamel*, Stockholm, 1931; Bevelander, G., *Anat. Rec.*, 1941, 81, 79 (formation of dentine).

[7] For dates of calcification of dental crowns, see Logan and Kronfeld, *Jour. Amer. Dent. Ass.*, 1933, 20, 379; Kronfeld, R., *ibid.*, 1935, 22, 1131; Hellman, M., *White House Conference Publications*, 1933, Pt. 2, p. 131; Harris, H. A., *Dent. Rec.*, 1936, p. 113 (Growth and Dentition); Broadbent, R. H., *The Angle Orthodontist*, 1937, 7, 24; Dick, J. Lawson, *Med. Press.*, 1917, 1, 309.

[8] Sprawson, E., *Brit. Dent. Jour.*, 1937, 62, 177.

[9] King, J. D., *Jour. Anat.*, 1939, 73, 424 (enamel of incisors of rat); see also references given in note [6].

[10] The cusps of premolar and molars are laid down in the positions they occupy in the fully developed crown, becoming united as the intervening field is calcified. There must be a mechanism for regulating the position of the cusps of the lower and upper teeth, so as to bring them into proper apposition.

[11] For recent work on nerve supply of dentine and peridental tissue, see Lewinsky and Stewart, *Jour. Anat.*, 1936, 70, 349; *ibid.*, 1937, 71, 233; Tiegs, O. W., *ibid.*, 1938, 72, 234; Sprenkel, H. B., *ibid.*, 1936, 70, 233.

[12] Mummery, J. H., *Phil. Trans.*, 1919, 209 (B), 305.

[13] Schour, I., *Jour. Amer. Dent. Ass.*, 1936, 23, 1946.

[14] Mellanby, Lady, *Trans. Obstet. Soc. Edin.*, 1938, p. 25; *Reports of Med. Resear. Coun.*, 1929, No. 140; Irving, A. and E., *Nature*, 1942, 150, 122.

[15] For evolutionary theories which seek to explain the form of human (and primate) teeth, see Gregory, W. K., *The Origin and Evolution of the Human Dentition*, 1922; Adloff, P., *Zeitsch. Anat. Entwickl.*, 1937, 107, 69; Remane, A., *Beitraege zu Morphologie des Anthropoidengebisses*, 1921; Keith, Sir A., *New Discoveries relating to the Antiquity of Man*, 1931.

[16] See McCown and Keith, note [27], Chapter XIII. We saw (p. 101) that in the segmentation of the body, characters of one segment may be transferred in part to an adjoining segment. It is also so with adjacent tooth buds; premolar characters may be transferred in part to a canine, or molar to a premolar.

[17] In case readers may wish to know Osborn's terms: in upper molars, *a.i.*, protocone; *a.e.*, paracone; *p.e.*, metacone; *p.i.*, hypocone. In lower molars: *a.i.*, metaconid; *a.e.*, protoconid; *p.e.*, hypoconid; *p.e'*, hypoconulid; *p.i.*, entoconid.

[18] Bolk, L., *Jour. Anat.*, 1921, 55, 138 *et seq.*

[19] Colyer, Sir J. F., *Variations and Diseases of the Teeth of Animals*, 1936.

[20] Keith, Sir A., *Proc. Roy. Soc. Med.*, 1913, 6 (odontol. sect.), 103; Keith and Knowles, *Jour. Anat.*, 1911, 46, 12; Shaw, J. C., *ibid.*, 1928, 62, 476.

[21] For recent literature on the eruption of teeth, see Brash, J. C., note [26], Chapter XIII (mechanism of eruption); Broadbent, R. H., *Anat. Rec.*, 1937, 68, 10; Hellman, M., *Internat. Jour. Orthodont.*, 1932, 18, 777; Goldstein and Stanton, *Human Biol.*, 1936, 8, 161; Brodie and Others, *The Angle Orthodontist*, 1938, 8, 261; Young and Others, *Special Reports Med. Resear. Coun.*, 1937, No. 225 (dates of eruption); Cattell, Psyche, *Jour. Dent. Res.*, 1928, 8, 279; Schultz, A. H., *Contrib. Emb.*, 1937, 26, 71 (in man and apes); Harris, H. A., See reference given in note [7].

[22] For irregularities of the 3rd molar teeth in eruption and in development, see Hellman, M., *Dental Cosmos*, 1936, 77, July; Henry C. Bowdler, *Biometrika*, 1936, 28, 378; Schultz, A. H., *Human Biol.*, 1934, 6, 627; Campbell, D. K., *Dental Cosmos*, 1934, 76, 459. One 3rd molar or more may be missing in only 3% of primitive peoples and up to 50% in civilized Europeans.

[23] The lower incisors pass behind " of mankind; the scissors-like bite of persistence of an infantile character. 1934, 34, 131.

[24] Keith, Sir A., "Growth of the Jaws," *Publications of the Dental Board*, 1924; Brash, J. C., *ibid.*, 1926, 1931 (see note [26], Chapter XIII); Harris, H. A., *Nature*, 1939, 144, 552.

[25] Frazer, J. E., *Manual of Embryology*, 1931, p. 277.

[26] Starkie and Stewart, *Jour. Anat.*, 1931, 65, 319.

[27] Harpman and Woollard, *Jour. Anat.*, 1939, 73, 112.

[28] Glasstone, S., *Jour. Anat.*, 1936, 70, 210; *Proc. Roy. Soc.*, 1938, 126 (B), 315; *Trans. Brit. Soc. Orthodont.*, 1938, p. 52; Huggins and Others, *Jour. Exper. Med.*, 1934, 60, 199.

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[14] Mellanby, Lady, *Trans. Obstet. Soc. Edin.*, 1938, p. 25; *Reports of Med. Resear. Coun.*, 1929, No. 140; Irving, A. and E., *Nature*, 1942, 150, 122.

[15] For evolutionary theories which seek to explain the form of human (and primate) teeth, see Gregory, W. K., *The Origin and Evolution of the Human Dentition*, 1922; Adloff, P., *Zeitsch. Anat. Entwickl.*, 1937, 107, 69; Remane, A., *Beitraege zu Morphologie des Anthropoidengebisses*, 1921; Keith, Sir A., *New Discoveries relating to the Antiquity of Man*, 1931.

[16] See McCown and Keith, note [27], Chapter XIII. We saw (p. 101) that in the segmentation of the body, characters of one segment may be transferred in part to an adjoining segment. It is also so with adjacent tooth buds; premolar characters may be transferred in part to a canine, or molar to a premolar.

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[18] Bolk, L., *Jour. Anat.*, 1921, 55, 138 *et seq.*

[19] Colyer, Sir J. F., *Variations and Diseases of the Teeth of Animals*, 1936.

[20] Keith, Sir A., *Proc. Roy. Soc. Med.*, 1913, 6 (odontol. sect.), 103; Keith and Knowles, *Jour. Anat.*, 1911, 46, 12; Shaw, J. C., *ibid.*, 1928, 62, 476.

[21] For recent literature on the eruption of teeth, see Brash, J. C., note [26], Chapter XIII (mechanism of eruption); Broadbent, B. H., *Anat. Rec.*, 1937, 68, 10; Hellman, M., *Internat. Jour. Orthodont.*, 1932, 18, 777; Goldstein and Stanton, *Human Biol.*, 1936, 8, 161; Brodie and Others, *The Angle Orthodontist*, 1938, 8, 261; Young and Others, *Special Reports Med. Resear. Coun.*, 1937, No. 225 (dates of eruption); Cattell, Psyche, *Jour. Dent. Res.*, 1928, 8, 279; Schultz, A. H., *Contrib. Emb.*, 1937, 26, 71 (in man and apes); Harris, H. A., See reference given in note [7].

[22] For irregularities of the 3rd molar teeth in eruption and in development, see Hellman, M., *Dental Cosmos*, 1936, 77, July; Henry C. Bowdler, *Biometrika*, 1936, 28, 378; Schultz, A. H., *Human Biol.*, 1934, 6, 627; Campbell, D. K., *Dental Cosmos*, 1934, 76, 459. One 3rd molar or more may be missing in only 3% of primitive peoples and up to 50% in civilized Europeans.

the 7th and 8th weeks the cavity of the pit is rapidly enlarged; free communication with the mouth is established; the nasal cavity has then become, as in amphibians, the functional vestibule of the respiratory system. In the 3rd month the palate is complete, and the stage peculiar to mammals thus established [1].

In tracing the development of structures subservient to the sense of smell, the following elements have to be dealt with: (i) the olfactory sense epithelium and olfactory nerves; (ii) the parts of the brain concerned with the sense of smell; (iii) the capsule which contains the olfactory epithelium; (iv) the respiratory tract of the nasal cavities.

(i) **Origin of the Olfactory Sense Epithelium.**—At the end of the 4th week, a small area of the ectoderm lying under the fore-brain becomes demarcated on each side, to form the *olfactory plates*. Around these two

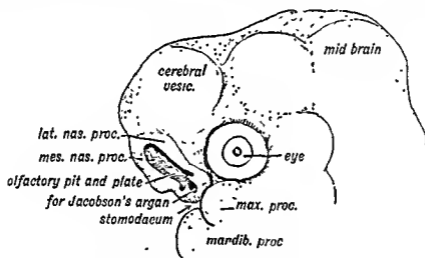


FIG. 233. The Olfactory Pit and Nasal Processes in a Human Embryo about 5 weeks old. (After Kollmann.)

plates the lateral and mesial nasal processes grow up (Fig. 233), the plates becoming at the same time invaginated to form the *olfactory pits*. With the growth of the nasal processes the cavities of the expanding olfactory pits or pockets come to occupy a space on the roof of the stomodaeum, their openings being turned towards that cavity. The ectodermal lining becomes the epithelial membrane of the nasal cavities. A small island is detached from each olfactory plate to form the basis of Jacobson's organ (Fig. 233). The sense epithelia in the olfactory area behave as nerve cells and, in the 6th week, send out nerve processes which establish contacts with initial or mitral cells in the olfactory bulbs. The olfactory nerves are thus formed. At first the olfactory plates are directly in contact with the cerebral vesicle, but later on they are separated by the formation of the cerebral membranes and epihriform plates (Fig. 187).

CHAPTER XV

THE NASAL CAVITIES AND OLFACTORY STRUCTURES

Evolution of the Nasal Cavities.—Although the sense of smell is a minor one in the economy of the human body, it is very evident that in the root-stock from which mammals have been evolved the olfactory organ must have held a foremost place amongst the sensory structures. We have seen that the great superstructure of the brain rests on the primary ganglia connected with the olfactory nerves. When we now examine the changes connected with the development of the nose and nasal cavities in the human embryo, we shall see, behind the complicated processes at work, a recapitulation of conditions which are to be seen

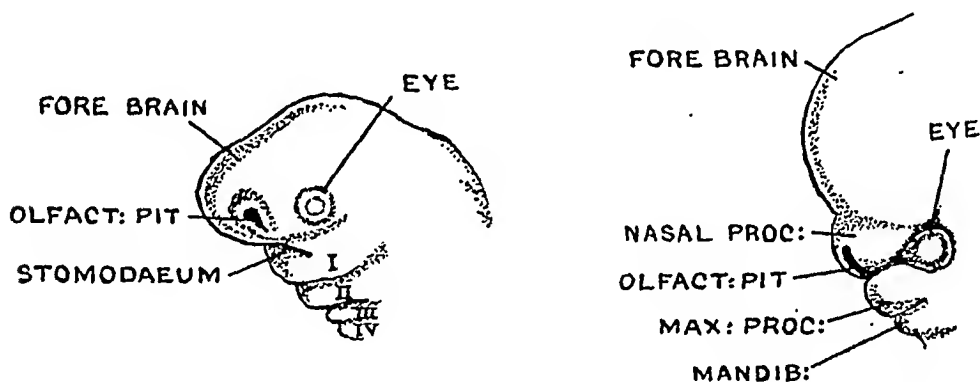


FIG. 232.

- A. The Olfactory Pit and Face of an Embryo in the 5th week of development. (After Broman.)
 B. The Olfactory Pit and Facial Processes in an Embryo in the 6th week of development. (After Hochstetter.)

in animals occupying a very low position in the vertebrate kingdom. At the end of the 4th week the olfactory membrane appears as two plaques of ectoderm in contact with the under surface of the fore-brain (Figs. 186, A, 232, A); in the 5th week the plaques or plates become two pits—right and left, the usual condition in fishes; in the 6th week each pit becomes connected with the primitive mouth or stomodaeum by a groove or fissure—a condition seen in the dog-fish; in the 6th and 7th weeks the pit is deepened and its opening becomes turned towards the stomodaeum owing to the forward growth of its lateral and mesial margins which form the lateral and mesial nasal processes (Fig. 186). The processes unite in the manner already described and a nasal cavity similar to that of the air-breathing or dipnoean fishes is established. In

cerebral vesicle is growing forwards to form the olfactory vesicles. At the end of the 3rd month the olfactory vesicle has assumed the form shown in Fig. 234. Its cavity is at first continuous with that of the cerebral vesicle, but this connection is lost in the 3rd month; it becomes solid, and forms the olfactory bulb and tract (Fig. 236). The tip of the anterior horn of the lateral ventricle marks the point at which the cavity of the olfactory lobe communicated with the cerebral vesicle.

The Rhinencephalon.—The Rhinencephalon is made up of the parts of the cerebrum which are primarily connected with smell. These parts are best seen in a typical mammalian brain such as is shown in Fig. 235.

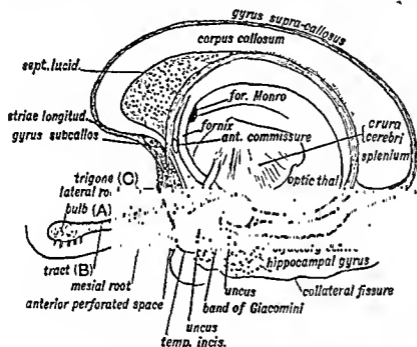


FIG. 236. The parts of the Rhinencephalon in the Human Brain.

They are, following the classification of Elliot-Smith: (i) the olfactory bulb and peduncle or tract, both of which are developed from the olfactory vesicle; (ii) the olfactory tubercle, represented in the human brain by a small area behind the trigone; (iii) the paraterminal body (Figs. 334, 335) which is represented in the human brain by the gyrus subcallosus and septum lucidum; (iv) the hippocampal formation represented in the human brain by the supra-callosal gyrus, the gyrus dentatus, hippocampus and fornix (Fig. 236); (v) the pyriform lobe (the uncus of the human brain); (vi) the anterior perforated space. In man these parts are reduced in size owing to (i) his sense of smell having become less acute; (ii) the great development of the corpus callosum and mantle of the brain. The rhinencephalon represents the

In the foetus the olfactory or sense epithelium is relatively extensive, as is the case in mammals with a keen sense of smell. It descends almost

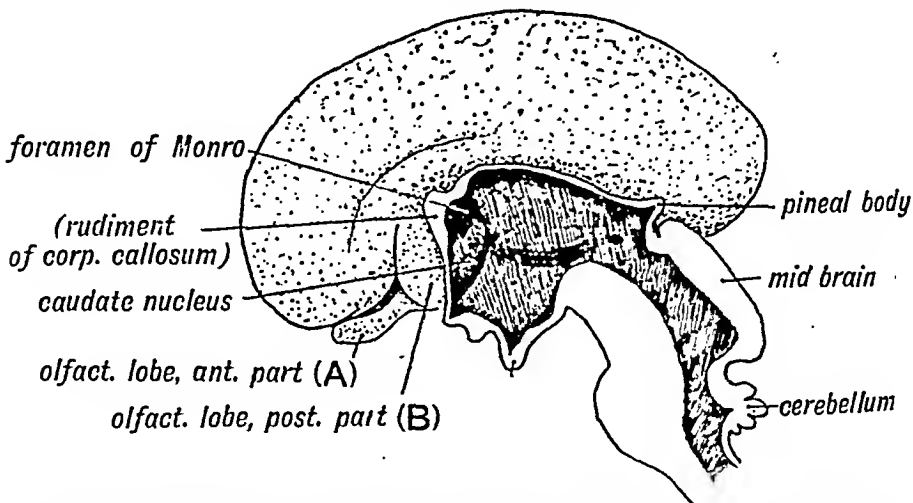


FIG. 234. The mesial aspect of the Brain of a Human Foetus 3½ months old, showing the Olfactory Lobc. A, olfactory bulb; B represents the paraterminal part of the rhinencephalon.

to the lower border of the middle turbinate on the outer or lateral wall, and to the junction of the upper two-thirds with the lower third on the

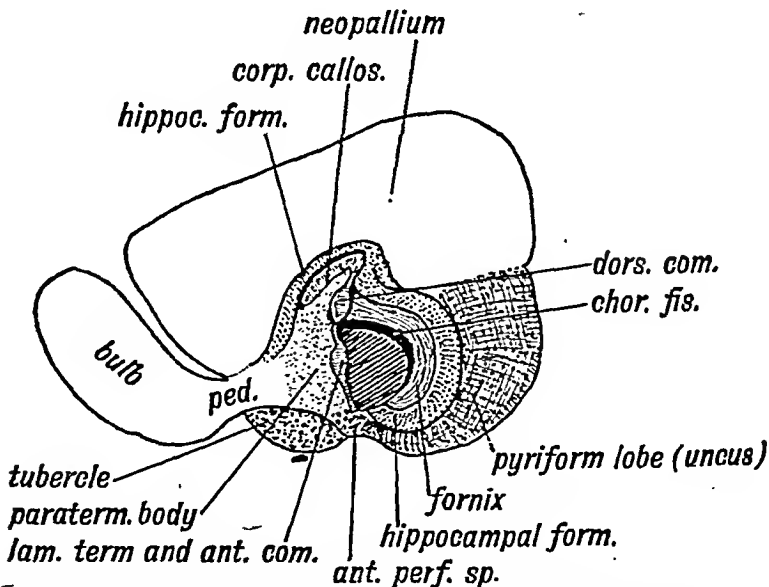


FIG. 235. The mesial aspect of a typical Mammalian Cerebrum showing the parts of the Rhinencephalon. (Elliot-Smith.)

mesial or septal wall. In the adult the distribution is much restricted—occupying areas only about one-finger's breadth in extent below the cribriform plate.

(ii) **Olfactory Bulb.**—As the olfactory pits are being thrust into the roof of the stomodaeum during the 6th week, a part of the floor of each

actually been formed in the walls of the primitive nasal cavities, linear outgrowths of the lining epithelium are observed to occur in the lateral wall and roof [3]. These outgrowths give rise to the meatuses of the nose—the inferior under the maxillo-turbinial appearing first, about the

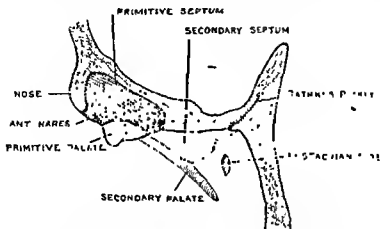


FIG. 237. The Primitive Nasal Cavities and Choanae at the end of the 6th week. The formation of the secondary septum and palate is indicated. (After Prof. J. E. Frazer.)

8th week, the superior last, about the 12th week. In the lateral wall of the nasal cavity of a foetus 20 mm. long and in the 8th week of development two linear depressions are present [4]—the lower representing the inferior meatus, the upper the *hiatus semilunaris* (ethmoidal

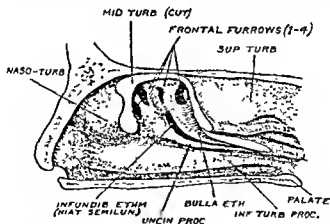


FIG. 238. The Lateral Wall of the Nasal Cavity of a child at birth. (J. Parsons Schaeffer.)

infundibulum, Fig. 238). The turbinate processes are developed out of the lateral wall and roof of the nasal cavity. The usual number is five in mammals, but in man the 4th and 5th are only temporary. The inferior or maxillo-turbinale is developed on the lateral wall, but the middle and upper appear at first on the roof and septal wall, their lateral

oldest part of the brain, and its grey matter differs from the rest of the cortex by the comparative simplicity of its structure.

Morphology of the Olfactory Neural Elements.—If the olfactory area of ectoderm were to adhere to and form part of the olfactory bulb, then the olfactory vesicle would be comparable with the optic vesicle, the rods and cones representing the olfactory epithelium, the ganglion cells of the olfactory bulb those of the retina, while the lateral and mesial olfactory tracts would correspond to the optic tracts. The homology, however, breaks down when we trace the olfactory tracts to their central connections. The fibres of the lateral root, unlike those of the optic tracts, end in a cortical formation, that of the uncus (Fig. 236). The fibres of the mesial root, on the other hand, like those of the optic tracts, end in basal nuclei, represented by the olfactory tubercle and the paraterminal body. From these nuclei relays carry olfactory stimuli to all parts of the hippocampal formation and to the hypothalamus. The commissural system of the fornix, both its transverse and its longitudinal fibres, serve to connect the various centres concerned with the sense of smell. The anterior commissure unites the right and left cortical areas of the rhinencephalon.

Nasal Cavities.—The nasal cavities are formed by the expansion of the olfactory pockets within the substance of the three developmental masses which surround each of them—the mesial nasal, lateral nasal and maxillary processes. When these processes unite in the 7th week, the primitive nasal cavity rapidly expands, and an opening temporarily closed by peridermal epithelium is reformed in its fundus or floor. This is the primitive choana, situated in the roof of the mouth (Fig. 205, p. 249). The choanae are separated by the primitive nasal septum, and are at first in front of the pituitary outgrowth—Rathke's pocket (Fig. 237). In the latter part of the 2nd month and the earlier half of the 3rd the primitive nasal septum and the choana on each side of it, extend their dimensions until the posterior border of the septum reaches and involves the mouth of Rathke's pocket [2]. In this manner the nasal septum is secondarily extended, and the nasal cavities greatly deepened (Fig. 237). At the same time the floor of the nasal cavities is prolonged backwards by the formation of the secondary palate, and the secondary choanae are established within the region of the naso-pharynx before the end of the 3rd month. The process of chondrification begins in the lower part of the lateral nasal process during the period at which the secondary palate is being formed. The chondrification of the lateral mass of the ethmoid and other parts of the olfactory capsule have already been described (p. 222).

Development of Turbinates and Air Sinuses.—Before cartilage has

actually been formed in the walls of the primitive nasal cavities, linear outgrowths of the lining epithelium are observed to occur in the lateral wall and roof [3]. These outgrowths give rise to the meatuses of the nose—the inferior under the maxillo-turbinal appearing first, about the

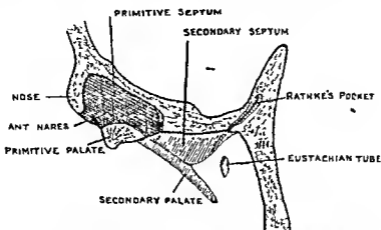


FIG. 237. The Primitive Nasal Cavities and Choanae at the end of the 6th week. The formation of the secondary septum and palate is indicated. (After Prof. J. E. Frazer.)

8th week, the superior last, about the 12th week. In the lateral wall of the nasal cavity of a foetus 20 mm. long and in the 8th week of development two linear depressions are present [4]—the lower representing the inferior meatus, the upper the *hiatus semilunaris* (ethmoidal

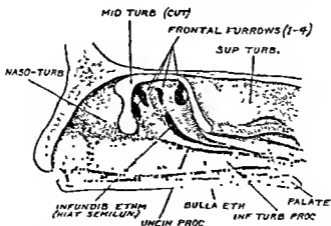


FIG. 238. The Lateral Wall of the Nasal Cavity of a child at birth. (J. Parsons Schaeffer)

infundihulum, Fig. 238). The turbinate processes are developed out of the lateral wall and roof of the nasal cavity. The usual number is five in mammals, but in man the 4th and 5th are only temporary. The *inferior or maxillo-turbinate* is developed on the lateral wall, but the middle and upper appear at first on the roof and septal wall, their lateral

position being attained in the course of development. The sphenoidal turbinate also belongs to the ethmoidal series, but becomes applied to the body of the presphenoid. The turbinates and meatuses are developed in connection with respiration. They increase, it is true, the olfactory area, but their chief use is apparently to filter and warm the inspired air.

The manner in which the nasal mucous membrane pushes its way from the middle meatus into the maxillary process to form the *antrum of Highmore* has been already described (p. 254). The other air sinuses—the frontal, lachrymo-ethmoidal, anterior, middle and posterior ethmoidal, and sphenoidal sinuses—six in all, arise in the same way as the antrum, but begin, with the exception of the last named, to enlarge at a much later date. Although they begin to bud out about the time of birth, they assume their active growth in the earlier years of puberty, and reach their full size before the 30th year.

At birth, the lateral mass of the ethmoid is a thin plate, carrying the superior and middle turbinate processes, which almost fill the nasal cavity (Figs. 204, 238). The entire ethmoid is narrow, and hence the proximity of the eyes in children. Beneath the middle turbinate is a thumbnail-like impression—the *hiatus semilunaris*, or ethmoidal infundibulum, one of the earliest formations (8th week). The maxillary sinus buds out near its posterior end, the point at which the bud arises becoming the site at which the sinus opens in the middle meatus (Fig. 239). The uncinate process of the lateral mass of the ethmoid forms the prominent lower margin of the hiatus (Fig. 238). A second opening for the sinus may be present below the level of the uncinate process, or this lower mouth may be the only one developed.

In Fig. 238 part of the middle turbinate has been removed to expose the *frontal recess* of the middle meatus—an expansion of the meatus formed in the 4th month of foetal life. At birth four furrows are present—representing the buds of air sinuses [5]. One, or occasionally two, of these enlarge to form the frontal sinuses, the others becoming cells of the ethmoid. The duct or mouth of the frontal sinus may become secondarily continuous with the hiatus semilunaris or the bud of the frontal sinus may arise from the upper end of the hiatus. The bud of the frontal sinus, as it expands, pushes its way into the frontal bone, separating the outer from the inner lamella. The bud is formed in the 1st year, but is nascent until the 5th. A second frontal bud may arise and partially or completely supplant the primary frontal outgrowth. As a rule, by the 25th year the sinus reaches outwards over the inner two-thirds of the orbital roof, and is an inch or more both in height and depth at its mesial part. It is smaller in women than in men, but it may

he, and often is, arrested at an early stage of development, or it may be absent altogether. The size of the supraciliary prominence is no index to its development.

The stalk of the frontal bud forms the infundibulum or naso-frontal duct, which is narrow, half an inch long, and difficult of catheterization from the nose. Into it open (or sometimes into the hiatus) the *lachrymo-ethmoidal* and *anterior ethmoidal cells* which surround the infundibulum. They are developed as outgrowths from the infundibulum (Fig. 239). Occasionally the maxillary sinus, as is frequently the case in the gorilla, sends a process to form part of the frontal sinus, and hence there may be a communication between the sinus and the antrum [6].

The development of the frontal sinuses and supra-orbital ridges leads

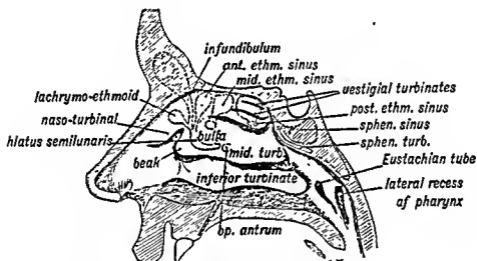


FIG. 239. A diagram of the Lateral Wall of the Nasal Cavity, showing the position of the Air Sinuses. The parts beneath the turbinate processes are indicated by stippled lines.

to a marked change in the face at puberty. By the formation of the frontal sinuses the basal area of the skull, to which the face is attached, is largely increased in extent. Such an increase is necessary to support the palate, which grows rapidly in size at puberty. Up to the 5th year the upper jaw has to carry only ten milk teeth; in the adult it has to carry sixteen permanent teeth. To support these the face and palate have to be enlarged. The formation of the frontal sinus gives the necessary increase in the area of the base of the skull for their support. It should be remembered that the growth of the brain and of the cranial cavity is comparatively slight after the 5th year. Only the gorilla and chimpanzee show an arrangement of frontal and ethmoidal sinuses comparable to that of man.

Above the hiatus lies the *bulla ethmoidalis*, which is inflated by and

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enclosed by a scroll of cartilage. It reaches its maximum development in the human foetus at the 5th month, and afterwards becomes a mere vestige—often unrecognizable. It sometimes persists and forms a very evident structure on the septum (Fig. 240). This special area of the olfactory organ is highly developed in all herbivorous vertebrates in which the naso-palatine canals are widely open, and thus the juices and odours of the mouth have free access to the organ. Prof. Broman has suggested that Jacobson's organ is for sampling substances dissolved in fluid, as is the case with the olfactory organ of fishes [8].

Nervus Terminalis.—Amongst the fibres of the olfactory nerve, particularly in the branch to Jacobson's organ, there occur nerve cells apparently of the same nature as those belonging to the sympathetic system. From these cells issue fibres which connect the olfactory areas

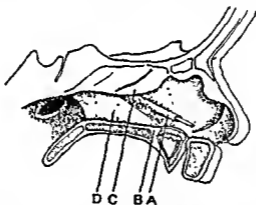


FIG. 240. Nasal Septum of a Child at Birth, showing a rod inserted in the pocket of Jacobson's organ (A). B, closed naso-palatine canal; C, presphenoid; D, vomer. (A. J. E. Cave)

of sense epithelium with grey matter near the lamina terminalis of the fore-brain. Besides these afferent fibres, there are also efferent, which arise from the parent nucleus in the paraterminal body. Both sets of fibres constitute the nervus terminalis, which is well developed in low vertebrates and of which there remains a vestige in man [9].

Nasal Duct.—Although in no way connected with the sense of smell, the nasal duct is closely related to the nasal cavities and must receive consideration here. It is formed between the lateral nasal and maxillary processes (Figs. 184, 233). It is laid down as a solid epithelial cord along the naso-maxillary groove at the end of the 2nd month. It becomes canaliculized during the 3rd month [10]. Three bones bound it: the superior maxilla on the outer side, formed in the maxillary process; the inferior turbinate, formed in the cartilage of the lateral nasal process, and the lacrymal, formed over the lateral nasal cartilage, bound it on the inner side. The formation of the palate cuts the duct

commonly carries the opening of the middle ethmoidal cell (Figs. 238, 239). The posterior ethmoidal sinus opens beneath the superior turbinate process, and is developed from the superior meatus. The *ethmoidal sinuses* are produced in the cartilage of the ethmoidal or lateral nasal plate (Fig. 210). They inflate the ossifying cartilaginous plate until it becomes a cellular mass, thus increasing the breadth of the intra-orbital septum. The *sphenoidal sinus* (Fig. 239) is formed during the 3rd month by the mucous membrane growing into and expanding the sphenoidal turbinate bone, which is a small, slightly ossified cartilage lying beneath the presphenoid at birth, and forming the uppermost (6th) of the nasal turbinate processes. In childhood the sinus grows into and expands the presphenoid and part of the basi-sphenoid, the sphenoidal turbinate remaining as its anterior wall. The sphenoidal turbinate is a detached part of the ethmoidal cartilage [7].

It will thus be seen that all the nasal air sinuses are produced primarily by a budding outwards of the nasal mucous membrane into the cartilaginous basis of the lateral nasal processes. Disease may readily spread to these sinuses from the nasal cavities. By means of the sinuses the area of the face is increased to support the adult palate bearing the permanent teeth. Most of them open on the respiratory tract of the nasal cavity. They are lined by ciliated epithelium and ventilated with every breath. They act also as resonance chambers.

Vestigial Turbinates.—There is frequently to be seen in the adult, one or even two secondary meatuses above the superior; these are constantly present in the chimpanzee and in mammals with a keen sense of smell. In the human foetus of four months six turbinates are usually present, besides secondary processes in the meatuses beneath them. The uppermost of these, the 6th, becomes the sphenoidal turbinate; the 5th disappears; the 3rd and 4th may remain separate or become united; the 1st and 2nd form the inferior or maxillo-turbinal and middle turbinate processes. The *agger nasi* (naso-turbinal, Fig. 238), in front of the attachment of the middle turbinate process, is a vestige of the naso-turbinal, a process well developed in most carnivora and animals with a keen scent. The uncinate process, which forms the lower border of the hiatus semilunaris, is continuous at its base with the naso-turbinal. Through the hiatus semilunaris acting as a gutter, the antrum may become a cesspool for a suppurating frontal sinus.

Organ of Jacobson.—Mention has already been made of the organ of Jacobson—situated on the nasal septum above the naso-palatine canals (p. 241). During development (Fig. 233) a part of the olfactory plate becomes detached, and is afterwards invaginated so as to form a minute tubular pocket in the lower anterior part of the septum. It becomes

enclosed by a scroll of cartilage. It reaches its maximum development in the human foetus at the 5th month, and afterwards becomes a mere vestige—often unrecognizable. It sometimes persists and forms a very evident structure on the septum (Fig. 240). This special area of the olfactory organ is highly developed in all herbivorous vertebrates in which the naso-palatine canals are widely open, and thus the juices and odours of the mouth have free access to the organ. Prof. Broman has suggested that Jacobson's organ is for sampling substances dissolved in fluid, as is the case with the olfactory organ of fishes [8].

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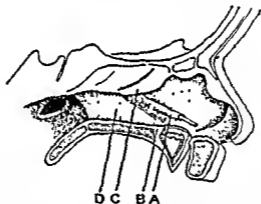


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off from the mouth. The hamulus of the lachrymal varies much in size, and is the vestige of a large process, which in lower primates enters into the formation of the inferior margin of the orbit. The *pars facialis* sometimes occurs in man (Fig. 241). Occasionally the frontal and superior maxillary bones may push towards each other between the

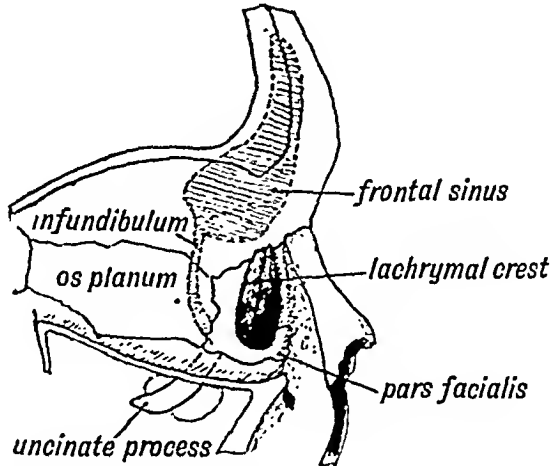


FIG. 241. Showing on the Inner Wall of the Orbit (1) the position of the Infundibulum, (2) the *pars facialis* lachrymalis.

lachrymal in front and lateral mass of the ethmoid behind, and thus form a fronto-maxillary articulation on the inner wall of the orbit.

Malformations of the Nose.—In Figs. 55, 189 and 201 two malformations of the nose are represented. In Fig. 189 the rare condition is shown in which one olfactory pit and its corresponding processes form a polypoid body; in Fig. 242 the condition of *cyclops*, where both nasal cavities are enclosed in a proboscis, is represented. The eyes are also fused. The condition of the facial skeleton in such a case is represented in Fig. 201. To bring about this condition there has been an arrest of growth of the cephalic end of the embryonic plate, with a fusion of the right and left olfactory bulbs and also of the optic vesicles [11]. The two olfactory plates and pits are united in a single median structure. Cyclops and allied conditions are to be regarded, not as reversions to ancestral stages of evolution, but as the result of injuries to the cephalic part of the neural plates during the earliest phase of their development. The cells of the neural crest of the head region are involved in the damage which gives rise to cyclops (see p. 240).

Two other malformations require mention. During the 3rd, 4th and 5th months of foetal life an epithelial plug is formed within the anterior nares—where the cutaneous and nasal epithelial coverings meet. In rare cases the plug becomes organized and forms a dense septum within

the nares. A similar obstruction, often containing bone, may be formed near the posterior nares. The posterior narial occlusion represents an organization and persistence of the epithelial membrane which at first

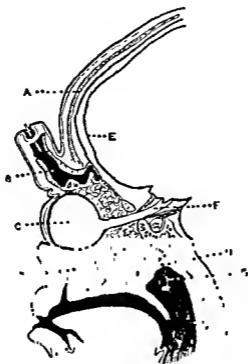


FIG. 242. Median sagittal section of the Head and Face in a case of Cyclops. A, frontal bone; B, single median nasal cavity contained in a proboscis formed by the nasal processes; C, median or fused eye; D, palate formed by the maxillary processes only; E, median cerebral vesicle; F, single optic nerve; G, Eustachian tube; H, palate bone.

closes the primitive choanae (see p. 286). Duplication of the nose is a rare abnormality. In such cases one or more of the nasal openings are blocked. The external nose may be absent (Mortimer Woolf).

NOTES AND REFERENCES

[1] For general works, see note [1], Chapter XIII. For special treatises, see Gluecksmann, A., *Zeitsch. Anat. Entwickl.*, 1934, 102, 480; Schneider, P. P., *ibid.*, 1935, 104, 61.

[2] See Frazer, J. E., *Manual of Embryology*, Chapter XV; Kelly, D. Brown, *Lancet*, 1, 157 (congenital occlusion of choanae).

[3] For development of air sinuses, see Jayle, G. E., *Ann. d'Anat. Path.*, 1935, 12, 876 (of ethmoidal cells); Myerson, M. C., *Archiv. Otolaryng.*, 1932, 15, 80 (variations in maxillary sinus); Sedgwick, H. J., *Amer. Jour. Roentgen. Rad. Therap.*, 1934, 32, 154 (variations in maxillary sinus). See also references given in note [22], Chapter XIII.

[4] Dickie, Milne, *Jour. Anat.*, 1914, 48, 445.

[5] Schaeffer, J. P., *Amer. Jour. Anat.*, 1916, 20, 125; *The Nose in Man*, Philadelphia, 1920.

[6] For nasal sinuses of anthropoids, see note [22], Chapter XIII.

[7] Fawcett, E., see note [6], Chapter XIII.

[8] For literature on Jacobson's organ, see note [12], Chapter XIII; also Brandt, W., *Jour. Anat.*, 1938, 72, 616; Roper-Hall, H. T., *Proc. Roy. Soc. Med.*, 1944, 38, 1 (Otol. Sect.); Bellairs, A., *Jour. Anat.*, 1942, 75, 157.

[9] For literature on the *nervus terminalis*, see Ariëns Kappers, note [3], Chapter IX; Pearson, A. A., *Anat. Rec.*, 1940, 76, 45 (suppl.); Larsell, Olaf, *Jour. Comp. Neur.*, 1918, 30, 1; Ayres, H., *ibid.*, 1919, 30, 323.

[10] For development of nasal duct, see Frazer, J. E., preceding note [2]; Mann, Ida, *Developmental Abnormalities of the Human Eye*, 1937; Politzer, G., *Zeitsch. Anat. Entwickl.*, 1936, 105, 329.

[11] For experimental production of Cyclops, see note [25], Chapter IV.

CHAPTER XVI

DEVELOPMENT OF THE STRUCTURES CONCERNED IN THE SENSE OF SIGHT

The Nature of the Eye.—It is in vain that we appeal to comparative anatomy for light on the various stages in the evolution of the eye; the eye of vertebrates is already fully formed in the earliest form known. Our knowledge of its origin and nature rests on an embryological foundation; during the 4th and 5th weeks of human development we see the eye compounded from three sources: (i) the retina and optic nerve arise as an outgrowth of the neural tube; (ii) the lens arises from the ectoderm or body covering; (iii) the tunics and mechanism of accommodation from the mesoderm. The union of these three tissues to form the most marvellous contrivance of the human body is a product of countless ages of evolution. A comparison with the olfactory organ, already mentioned in the last chapter, assists us in understanding the peculiar nature of the eye. The olfactory plates are neural in nature; their sensory cells give rise to the fibres of the olfactory nerves. The plaques of olfactory epithelium are situated near the open anterior end (neuropore) of the neural tube; one can easily understand how they might shift towards the neural tube, merge with it, and become incorporated within the part which forms the olfactory bulb. Were we to implant the olfactory epithelium in the olfactory bulb, we should produce a structure comparable to the retina. During an early part of the 4th week the two retinal plates are represented by depressions on the sides of that part of the medullary folds which, when enclosed, forms the fore-brain (Fig. 243). The epithelium which lines the optic evaginations, clearly parts of the original surface covering of the embryo, does not become ependymal cells, but, like the olfactory plates, gives rise to those highly modified sensory cells—rods and cones. Besides the rods and cones the epithelium of the optic evaginations gives rise to nerve and other cells, in this respect resembling a typical part of the neural tube. It is thus clear that the olfactory and optic nerves are of a totally different nature from other cranial nerves.

Binocular Vision.—In the course of the evolution of the Primates—the order to which man belongs—the structures connected with sight underwent a remarkable series of changes: (i) a minute area of each retina became modified to form the macula—a centre of acute vision; (ii) the

orbits were so altered that both eyes became directed forwards; (iii) nerve centres and muscles became capable of accommodation; (iv) a large area of the occipital cortex became modified for the receipt of impulses from the retina. We do not know how these structural changes were initiated and brought about, but their advantage to arboreal animals is very evident. Animals which use their hands and arms as means of arboreal progression must be able to judge accurately the distance from branch to branch; stereoscopic vision becomes a necessity for them [1]. We shall note the developmental processes which bring about these structural modifications as we proceed.

The structures concerned in the sense of sight are: (i) the Eyeball and the Optic Nerve; (ii) the Eyelids and Lachrymal Apparatus;

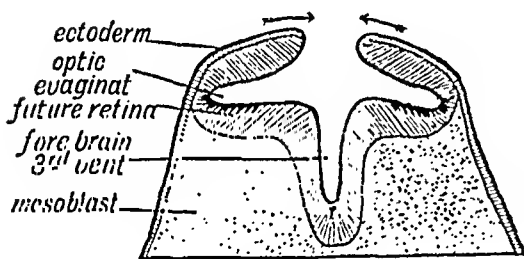


FIG. 243.

FIG. 243. Diagrammatic section across Fore-brain of a Human Embryo in early part of 4th week to show the Optic Evaginations. (After Prof. Bryce.)

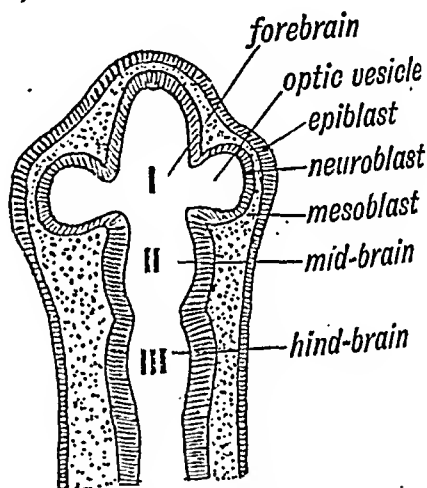


FIG. 244.

FIG. 244. Diagram of the Elements which form the Eyeball.

(iii) the Orbit, and the Muscles, Nerves and Vessels contained in it; (iv) the Nerve Centres and Tracts. We shall take up the consideration of these parts in the order just named.

The Eyeball.—The condition of the eye in the 4th week of foetal life is shown diagrammatically in Figs. 243, 244. The three elements which unite to form the eyeball are as yet separate. They are: (i) *Ectoderm*, which forms (a) the epithelium of the cornea, (b) the lens, and (c) the capsule of the lens. (ii) *Neuroderm*, which forms (a) the optic nerves, (b) sensitive retina, (c) pars ciliaris retinae, (d) uvea, (e) pigmentary layer of retina, (f) the hyaloid membrane and vitreous. (iii) *Mesoderm*, which forms: (a) outer tunic (sclerotic and fibrous cornea); (b) middle tunic (choroid, ciliary-choroid and the anterior stratum of the iris); (c) the hyaloid artery [2].

The chief Structures derived from the Ectoderm are : (a) *The lens*.—The lens is developed by a saecular invagination of the ectoderm situated over the optic vesicle at the beginning of the 5th week (Fig. 245). About a week later it becomes a closed sac by the severance of its connection with the ectoderm, its wall being formed by a single layer of epithelial cells [3]. The cavity of the lenticular vesicle is soon obliterated by the cells of the posterior wall becoming elongated (Fig. 246) until they reach

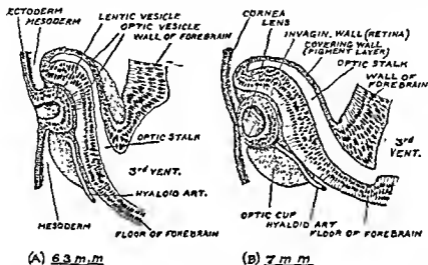


FIG. 245.

- A. Depression of the Ectoderm to form the Lenticular Vesicle, early in the 6th week. (Hochstetter.)
 B. Separation of the Vesicle later in the 6th week. Both figures represent Coronal sections of the fore-brain and optic vesicle of a human embryo. (After Hochstetter.)

the anterior wall (7th and 8th weeks). Each elongated cell is transformed into a lens fibre. The power possessed by the tissues of the optic cup of { "inducing" the overlying ectoderm to invaginate and form a lens has already been mentioned (p. 64).

The cells of the anterior wall retain their primitive form (Fig. 246). New lens fibres are added by the cells at the margin (equator) becoming multiplied and elongated. The central fibres, which are formed first, are the shortest, the fibres of every additional layer produced become longer than those of the previous layer, hence the concentric arrangement of fibres. Further, the fibres of each layer are so graduated in length that, when produced, they meet along certain lines which radiate from the anterior and posterior poles of the lens. The lens is relatively large at birth, being two-thirds of its final size; growth continues until puberty, and even then has not ceased, for Priestley Smith found that there is an appreciable addition to its weight with each decade of life. It will thus be seen that the lens is an area of modified epidermis,

orbits were so altered that both eyes became directed forwards; (iii) nerve centres and muscles became capable of accommodation; (iv) a large area of the occipital cortex became modified for the receipt of impulses from the retina. We do not know how these structural changes were initiated and brought about, but their advantage to arboreal animals is very evident. Animals which use their hands and arms as means of arboreal progression must be able to judge accurately the distance from branch to branch; stereoscopic vision becomes a necessity for them [1]. We shall note the developmental processes which bring about these structural modifications as we proceed.

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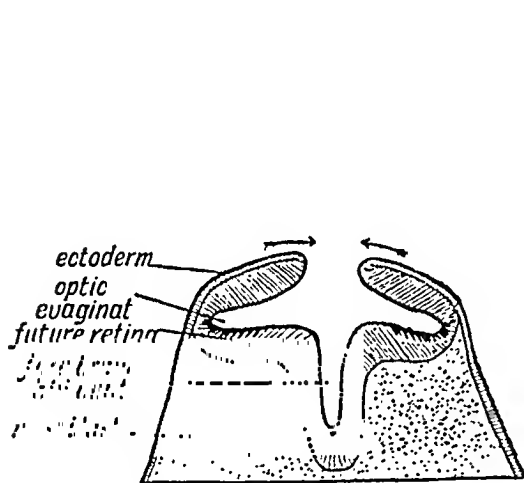


FIG. 243.

FIG. 243. Diagrammatic section across Fore-brain of a Human Embryo in early part of 4th week to show the Optic Evaginations. (After Prof. Bryce.)

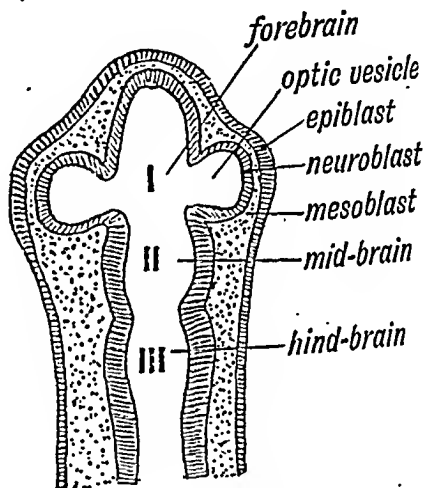


FIG. 244.

FIG. 244. Diagram of the Elements which form the Eyeball.

(iii) the Orbit, and the Muscles, Nerves and Vessels contained in it; (iv) the Nerve Centres and Tracts. We shall take up the consideration of these parts in the order just named.

The Eyeball.—The condition of the eye in the 4th week of foetal life is shown diagrammatically in Figs. 243, 244. The three elements which unite to form the eyeball are as yet separate. They are: (i) *Ectoderm*, which forms (a) the epithelium of the cornea, (b) the lens, and (c) the capsule of the lens. (ii) *Neuroderm*, which forms (a) the optic nerves, (b) sensitive retina, (c) pars ciliaris retinae, (d) uvea, (e) pigmentary layer of retina, (f) the hyaloid membrane and vitreous. (iii) *Mesoderm*, which forms: (a) outer tunic (sclerotic and fibrous cornea); (b) middle tunic (choroid, ciliary-choroid and the anterior stratum of the iris); (c) the hyaloid artery [2].

(c) The capsule of the lens is a cuticular membrane formed by the lenticular cells. Fine fibrils, similar in origin to the substance of the vitreous, are added to the capsule. They are formed between the margin of the optic cup and circumference of the lens; these give rise to the zonular membrane (Fig. 246). Outside the proper capsule a vascular tunic is formed from the mesoderm (Fig. 247).

Structures formed from the Optic Vesicles (neurodermal element).—Each vesicle is being demarcated into its several parts soon after the commencement of the 4th week; even before the medullary plates have met to enclose the cavity of the fore-brain the optic vesicles have commenced as evaginations of those plates (Fig. 243). They form a great lateral diverticulum on each side of that part of the fore-brain

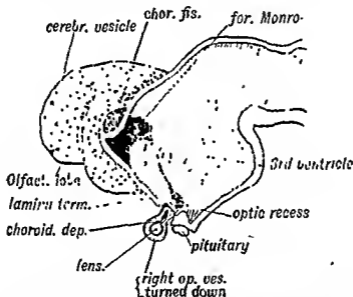


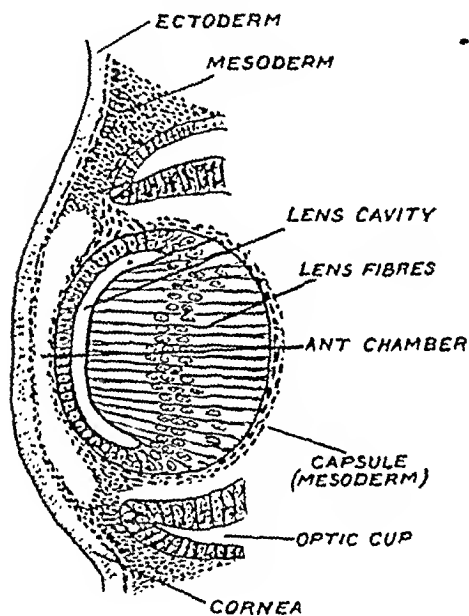
FIG. 248. Diagram showing the connection with the Fore-Brain and condition of the Optic Stalk and Vesicle at the end of the 6th week of development. (After Rus.)

which becomes the 3rd ventricle. The condition of the right optic vesicle at the end of the 6th week is shown diagrammatically in Fig. 248. The stalk or neck remains constricted to become the optic nerve while the vesicle enlarges and becomes invaginated to form the optic cup.

Invagination of the Optic Vesicle.—Almost as soon as it begins to grow out the optic vesicle becomes invaginated, one half being drawn within the other (Figs. 245, A, B). The lenticular bud lies within the indentation. The remarkable fact was discovered by Dr. Warren Lewis that the optic vesicle, if transplanted, can cause overlying ectoderm to produce a lenticular bud [5]. The invaginated vesicle is known as the optic cup. Fine fibres unite the neuroblastic cells which line the optic cup

and in manner of development closely resembles the sense organs in the skin of fishes and amphibians. Like the epidermis, it shows a tendency in the aged to be transformed into keratin. The oldest cells (the central or nuclear fibres) alter first; hence the central position of the cataract which occurs so frequently in old people.

(b) *The cornea.*—The epithelial covering of the cornea is continuous with the surrounding ectoderm. Like all embryonic tissues, the cornea is transparent, but it differs from them in retaining its transparency. Towards the end of the 2nd month the connective tissue of the cornea, the anterior chamber of the eye, the pupillary membrane and the vascular



16 m.m.

FIG. 246.

FIG. 246. The Formation of the Lens Fibres from the epithelium on the posterior wall of the lenticular vesicle and the ingrowth of mesoderm to form the substance of the Cornea and Vascular Capsule of Lens, 7th week. (After Lindahl.)

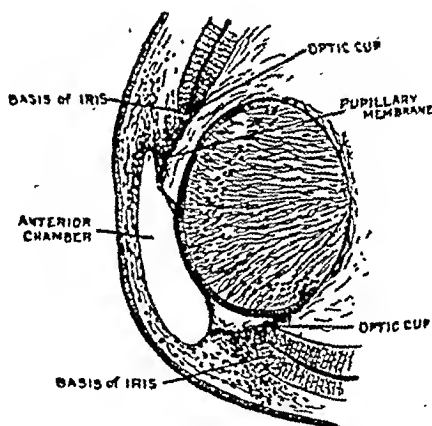


FIG. 247.

FIG. 247. Diagrammatic section of the Anterior Part of the Eyeball to show the state of the anterior chamber and iris in the 5th month. (After Broman.)

capsule of the lens are fashioned in the following manner. Mesoderm surrounding the optic cup invades the space between the ectoderm of the cornea and the lens, thus separating these two structures. In the midst of the invading mesoderm appears a cleft; this becomes the anterior or aqueous chamber of the eye (Figs. 246, 247). The mesoderm in front of the chamber provides the connective tissue basis of the cornea, while the mesoderm behind the chamber becomes the pupillary membrane and vascular capsule of the lens. Bowman's membrane is formed by a condensation of the tissue immediately under the epithelial covering of the cornea during the 5th month; a little later, the deepest stratum condenses into the membrane of Decemet [4].

(c) The *uvea* is the layer of pigmented epithelium which covers the posterior surface of the iris. It is formed out of both outer and inner layers of the optic cup, and represents the rim of the cup (Fig. 251).

(d) The *pars ciliaris retinae* is formed out of that part of the inner or

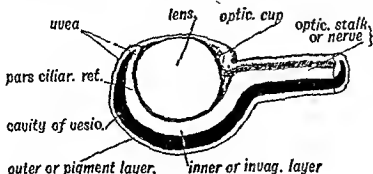


FIG. 250 Diagrammatic section of the Optic Cup and Lens. The cavity is represented as gaping, whereas from the 5th week onwards the outer and inner walls are in contact.

invaginated layer of the optic cup which lies in the shadow of the iris, and is therefore inaccessible to light rays. It also retains the primitive columnar or partly transitional form of the epithelium (Fig. 251). The *ora serrata* marks the junction of the *pars ciliaris retinae* and sensitive retina.

Ciliary Process.—At the commencement of the 4th month, the *pars*

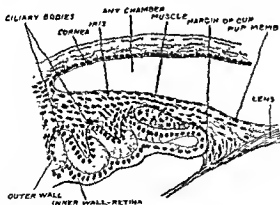


FIG. 251. Section of the Iris, showing the folding of the marginal part of the optic cup to form the ciliary processes and the origin of the sphincter muscle of iris from the anterior or outer layer of cup, in a Human Foetus of 6th months. (Szily.)

with the deep aspect of the lenticular vesicle (Cirincione). The invagination of the vesicle, which takes place in an oblique manner—as if pressure had been applied from below and behind—leads to the closure not only of the cavity of the vesicle, but also to that of the distal half of the stalk (optic nerve). The point at which the central artery enters the optic nerve marks the upper limit of the invagination of the optic stalk (Fig. 249). By the end of the 5th week the optic vesicle no longer communicates with the cavity of the fore-brain, but the recessus opticus in the floor of the 3rd ventricle, above the chiasma, remains to mark the point at which the original evagination took place (Fig. 248). The parts formed from the optic vesicles are :

(a) The *optic nerve* is formed from the stalk of the optic vesicle. The wall of the stalk is at first composed of a single layer of columnar epithe-

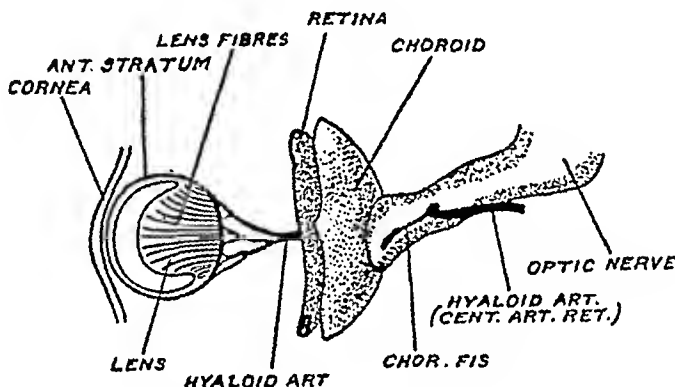


FIG. 249. Certain parts of the Eye during the 7th week of development. (After His.)

lium ; in the 2nd month these cells produce a sponge-work of fibres on the surface of the stalk [6]. During the 7th week, the optic fibres, developing as processes of the neuroblasts of the invaginated layer, begin to grow into the brain from the retina along the sponge-work of the optic stalk [7]. Thus are formed the greater number of the fibres in the optic nerve, there being over a million of fibres from each retina at birth [8]. The optic fibres also form the chiasma in the floor of the 3rd ventricle and the optic tracts on the wall of the fore-brain (Fig. 268). It will thus be seen that the optic nerves and vesicles are of the same origin as the cerebral vesicle—both representing modified parts of the wall of the fore-brain.

(b) The *pigmentary layer of the retina* is formed from the ensheathing or outer layer of the optic cup (Fig. 250). At first the wall of the optic vesicle is composed of a single layer of epithelium ; the outer or pigmentary layer of the retina retains this embryonic form. Pigment appears as early as the 6th week, commencing at the marginal border.

of development, is not fully differentiated until three months after birth. The original or ependymal layer, while dividing and producing broods of cells, still retains its position, the daughter cells being pushed towards the vitreous aspect of the retina, and by the middle of the 7th month of foetal life all the retinal elements are present, arranged in the same strata as in the adult. The retina is complete and sensitive to light by the end of the 7th month, but, as just said, the fovea centralis and macular area are not in action until three months after birth [10].

On each surface of the retina is developed a cuticular or *limiting membrane*. Some of the original epithelial (ependymal) cells become elongated between the limiting membranes and form the fibres of Muller (Fig. 252, *D*). On passing from the margin of the cup to its centre all stages in the development of the retina will be seen between the single layer and the multi-stratified condition (Fig. 252). Ulti-

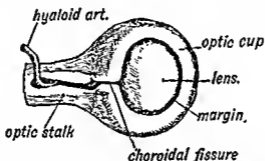


FIG 253. The Optic Stalk and Cup, viewed on the lower and lateral aspect, showing the choroidal fissure and free margin of the cup

mately three strata can be recognized in the retina. Beneath the outer limiting membrane the original cells remain as the retinal sense epithelium; processes from these cells break through the outer limiting membrane to form the rods and cones; the middle stratum forms bipolar cells; beneath the inner limiting membrane ganglionic cells are formed. The middle stratum by its processes links together the sense epithelium and the ganglionic cells, and thus stands in the same relationship to the sense epithelium and ganglionic cells as a posterior root ganglion does to the touch corpuscles of the skin and the cuneate and gracile nuclei of the medulla. In many respects the development of the retina recalls the development of the spinal cord. Both are formed from parts of the neural tube.

Choroidal Fissure.—Occasionally a congenital fissure is present in the lower segment of the iris (coloboma iridis) or choroid (coloboma choroidea) (Fig. 256). A white line, due to absence of pigment, may be seen in the corresponding segment of the retina when the interior of the eye is examined. These are due to imperfect closure of the choroidal fissure.

epithelium which covers the ciliary processes is secretory in nature. It forms the aqueous humour, thus recalling the ependyma, which covers the choroid plexuses of the ventricles of the brain. It is strange that from the same layer as gives origin to nerve cells there should also arise supporting (neuroglial) and secretory cells, and as we shall see anon, the unstriated muscle of the iris (Fig. 251).

(c) The *sensitive retina* is formed out of the inner or invaginated layer of the optic cup (Fig. 252). At first the inner wall is composed of a single layer of epithelium. The ciliary part of the retina retains this form. What is called the *outer* aspect of the primitive retina is directed

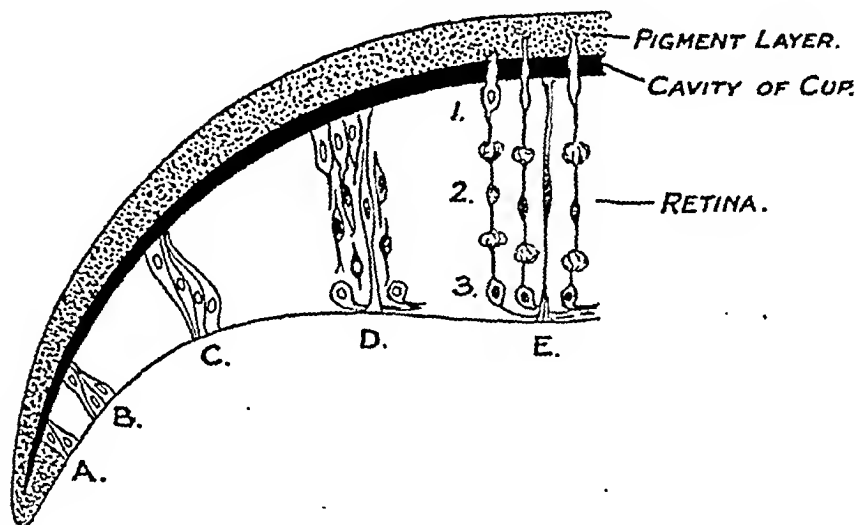


FIG. 252. Diagrammatic section across Optic Cup to show the manner in which the cells of the inner layer of the optic cup are differentiated to form the retina. (After Fürst.)

A, B, C, D, E, show stages in the development of the retina from the simple layer of cells.

1. The outer stratum of sense cells (rods and cones).
2. The middle stratum connecting (bipolar) nerve cells.
3. The inner stratum of ganglionic cells and fibres.

The cavity of the optic vesicle, which is closed by the invagination of the retinal layer within the cup and obliterated by the outgrowth of the rods and cones, is represented by a wide black zone in the diagram.

towards the pigmented layer, but is separated from that layer by what remains of the cavity of the optic vesicle (Fig. 250). That cavity, it will be remembered, is a prolongation of the neural canal or ventricular cavity of the brain. The sense cells of the retina, the rods and cones, therefore occupy the position of the lining ependyma of the ventricles of the brain. The *inner* or vitreous aspect of the retina, corresponding to the outer aspect of the neural tube, is directed towards the lens. The manner [9] in which the complicated strata of the retina arise from the single layer is represented diagrammatically in Fig. 252. Differentiation starts at the centre of the optic cup and spreads towards the periphery, but the *fovea centralis*, although becoming apparent in the 3rd month

epithelium, which remains *in situ*, and the rods and cones, which fall inwards with the nerve layer. Fluid then collects in the site of the primitive cavity of the optic vesicle. The optic part of the medullary plate of amphibian embryos has been transplanted and produced a



FIG. 256.

FIG. 256. Coloboma or Cleft of Iris (After Seggel)

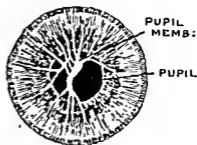


FIG. 257.

FIG. 257. Remains of Pupillary Membrane (After Prof Hippel)

retina in its new site. The retina has also been successfully grown in artificial media [11].

The Vitreous Body.—Dr. Ida Mann [12] distinguishes three stages in the development of the vitreous body; they are illustrated in Figs. 258, *A*, *B*, *C*. Up to the 7th week (*A*) the vitreous is represented by a

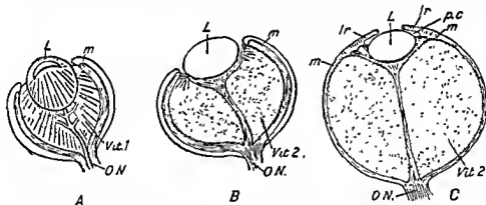


FIG. 258 Three stages in the development of the Vitreous Body. (After Dr Ida Mann)

A. Section of the optic cup of a human foetus in the 7th week of development.

B. Section of the cup about the middle of the 3rd month.

C. At the end of the 4th month.

vit 1, primary vitreous; *vit 2*, secondary or permanent vitreous; *O.N.*, optic nerve; *m*, margin of the primary optic cup; *pc*, posterior chamber; *Ir.*, iris and ciliary processes produced from primary margin; *L*, lens.

system of fine fibrils which connect the inner limiting membrane of the retina with the capsule of the lens, all of them being ectodermal or neurodermal in origin. The only structure within the optic cup which is of mesodermal origin is the hyaloid artery. That artery issues from the optic disc to end in branches round and behind the lens. The sheath

The choroidal fissure is the result of the peculiar mode in which the optic vesicle is cupped or invaginated. The lens grows into it from the malar or lower lateral aspect and becomes lodged in the anterior part of the depression. The margins of the invagination grow over, and include, the hyaloid artery and meet as is shown in Fig. 253, their line of contact constituting the *choroidal fissure*. The margins of the fissure unite (Fig. 254); union begins near the centre of the fissure and spreads distally to the margin of the cup and proximally to the point of entrance of the hyaloid artery (Fig. 249). By the 8th week all trace of the fissure should have disappeared. The union recalls the closure of the fissure of the upper lip and of the margins of the neural tube. There is this

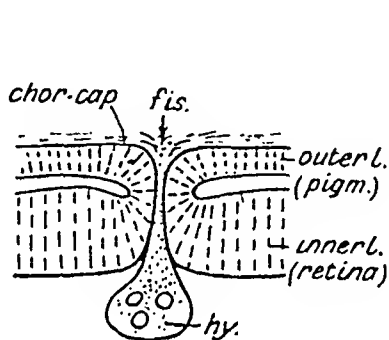


FIG. 254.

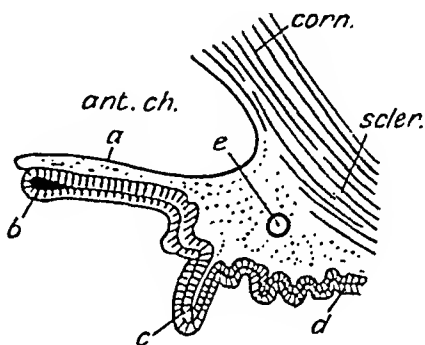


FIG. 255.

FIG. 254. Section across the Choroidal Fissure (*fis.*) to show the retinal lips being approximated so that the outer (pigmented) layer is brought against the outer layer and the inner against the inner. (After Dr. Ida Mann.) A remnant of the hyaloid vessels and tissue is shown included within the cup. The beginning of the capillary layer of the choroid is depicted (*chor. cap.*).

FIG. 255. Section of the Iris at the 5th month of development. (After Dr. Ida Mann.) The anterior margin of the optic cup has grown forward to provide the inner stratum of the iris and to form the covering of the ciliary processes.

a, anterior or mesodermal stratum of iris; *b*, remnant of the cavity of the optic cup; *c*, ciliary process; *d*, pars ciliaris retinae; *e*, circular vessel in which the ciliary arteries end; *ant. ch.*, anterior chamber; *corn.*, cornea; *scler.*, sclerotic tunic.

difference, however; in coloboma no open fissure remains, only a white line destitute of pigment. With the closure of the choroidal fissure the optic cup is completed, with one exception. Towards the beginning of the 4th month of foetal life, the margin of the cup takes on a special growth, expanding forward to provide the uveal coat for the iris (Fig. 255). The fissure shown in the iris (Fig. 256) is due to a failure of a narrow segment of the cup to take part in this forward expansion.

The primitive cavity of the optic vesicle (Fig. 250) is of some clinical importance. It is obliterated by the invagination of the vesicle; the rods and cones formed in the inner or invaginated layer grow out across the cavity into the outer or ensheathing pigmented layer of the retina (Fig. 252). From accident or disease the retina may be detached, thus causing blindness; the separation takes place between the pigmented

the 3rd month, taking its origin within the optic nerve from the stem of the hyaloid. The pathway in the vitreous which was occupied by the hyaloid artery remains as a passage or canal, the *hyaloid canal*. In cats and rabbits the hyaloid artery persists for some days after birth. Remnants may persist in the human eye and so interfere with vision.

The aqueous chamber is formed between the cornea and lens, its walls being entirely of mesodermal origin. In Fig. 259 the mesoderm which invades the space between the ectoderm and lenticular vesicle is represented as forming not only the basis of the cornea but also the anterior wall of the vascular tunic of the lens, these two parts being supposed to become separated by the formation of the aqueous chamber. Dr.

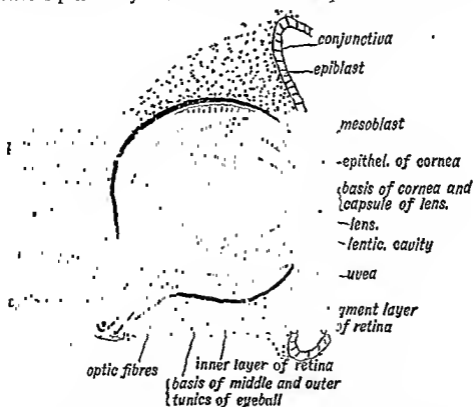


FIG. 259. Diagrammatic section of the Eye showing the parts formed from the mesoblast or mesoderm (After Hla's model of the eye of a 3rd-month human foetus)

Lindahl [13] is of opinion, however, that these two parts are formed separately, the mesodermal basis of the cornea in the 6th week and the lenticular capsule later, at the 9th week, the aqueous chamber being the potential chamber between these two formations (Fig. 246). We have seen how the forward growth of the anterior margin of the optic cup (Fig. 258, C) gives rise to the posterior compartment of the aqueous chamber. Fluid begins to collect in the pupillary area of this space in the 6th month and spreads, so that in the 7th month the chamber has

of the hyaloid artery corresponds to pia mater and is probably of neurodermal origin. By the end of the 3rd month (*B*) the permanent vitreous has begun to appear; it is a gel formed apparently by, and on, the inner surface of the retina. As the true or secondary vitreous accumulates, the primary material becomes compressed into a central strand extending from the disc to the vascular capsule of the lens (Fig. 258, *B*). The central strand carries the hyaloid artery. In the third and final phase (*C*), reached in the 4th month, the vitreous body has grown in volume; the chamber has been enlarged by the forward growth of the margin of the cup, and at the same time the circumference of the pupil is delimited. With the formation of the iris and of the ciliary bodies there come into existence, as may be seen in Fig. 258, *C*, a series of radial fibrils passing from the ciliary bodies to the circumference of the lens and of its capsule. These form the zonule of Zinn and the suspensory ligament of the lens. The structures just named bound the vitreous chamber in front and are of the same nature as the fibrils of the primary vitreous. With the formation of the iris another important structure comes into existence, namely, the posterior chamber, into which the aqueous exudes (Fig. 258, *C*, *p.c.*).

Parts of the Eyeball formed from Mesoderm.—As the optic cup represents an extension of the brain we expect it to be provided with corresponding coverings. We may rightly regard the choroid coat, with its rich vascular stratum (chorio-capillaris), as representative of the pia-arachnoid. The choroid begins to be laid down in the latter part of the 2nd month, to be followed in the 3rd month by a differentiation of the sclerotic, a fibrous coat which corresponds to the fibrous capsule of the skull, including the dura mater as part of that capsule. Under certain pathological conditions bone may form in the sclerotic.

The wall of the anterior chamber of the eye is pervaded by mesodermal structures. Mesoderm provides the fibrous coat of the cornea, the anterior stratum of the iris and the pupillary membrane.

The hyaloid artery, also of mesodermal origin, ends in the vascular capsule of the lens, providing that structure with nourishment during the period of its most active growth—the 3rd and 4th months of foetal life. After the 4th month the artery undergoes reduction and by the 6th month should be represented by a mere thread. As the anterior margin of the optic cup grows forward to form the iris in the 4th month, it lifts the anterior part of the vascular capsule from the lens, carrying it on the anterior surface of the iris; this anterior part now receives the name *pupillary membrane* (Fig. 257). Normally the pupillary membrane becomes absorbed in the 7th month.

The central artery of the retina becomes manifest towards the end of

recalling the deposition of dermal bones in the primitive capsule of the brain.

The *tapetum lucidum* is absent in the human and primate eye. It gives the metallic lustre seen on the retinal surface of the eye of the ox, and is formed by a layer of fine fibres which are developed on the retinal surface of the choroid.

The *capsule of Tenon*, the bursa or connective-tissue socket of the eyeball, is developed in the mesoderm surrounding the eyeball. A lymph space separates it from the sclerotic, which, however, is not clearly differentiated until after birth [14]. The *choanoid muscle* (retractor bulbi or orbital muscle), which surrounds the sclerotic part of the eyeball as a muscular hood in mammals and vertebrates generally and arises in

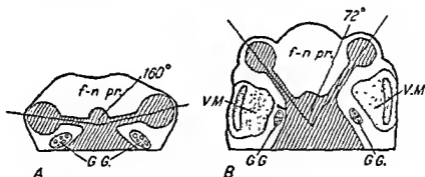


FIG. 261.

A. Section of the Head of a Human Embryo, 9 mm. in length and in the 6th week of development, showing that the ocular axis is almost at a right angle to the mid-line of the head (Frazer and Mann)

B

common with the external rectus, has become greatly reduced in man and the higher primates. Remains of the retractor bulbi—a striated muscle—have been described by Prof. Whitnall in the human orbit [15]. The *unstriated muscle of the orbit* occurs in two places; the *orbital part* (Müller's muscle) bridges the spheno-maxillary fissure; in man this is a mere vestige [16]; the palpebral part forms the non-striated musculature found in the insertions of the levator palpebrae. The non-striated muscle is supplied by sympathetic nerves. Its function is obscure.

The Binocular Angle.—One of the more striking events in the development of the human eye is the change which takes place in the ocular axis [17]. During the 6th week the axes of the eyes are set almost at right angles to the mid line of the head, the binocular angle being 160° (Fig. 261, A). Three weeks later (Fig. 261, B) the eyes have swung forwards, so that the binocular angle is reduced to 72° ; the angle in

extended to the corneo-scleral junction. Almost up to the time of birth, the anterior chamber of the aqueous is very shallow (Fig. 260), the lens lying near the cornea. Even in the 5th foetal month (see Fig. 247) the posterior part of the aqueous chamber—the part which lies between the iris and the lens—is not opened up. We must regard the aqueous system as strictly comparable to the cerebro-spinal and not as part of the lymph system.

The choroid, the vascular basis of the ciliary bodies, the stroma and vessels of the iris, all of mesodermal origin, provide a vascular covering for those parts of the eyeball which are derived from the optic cup,

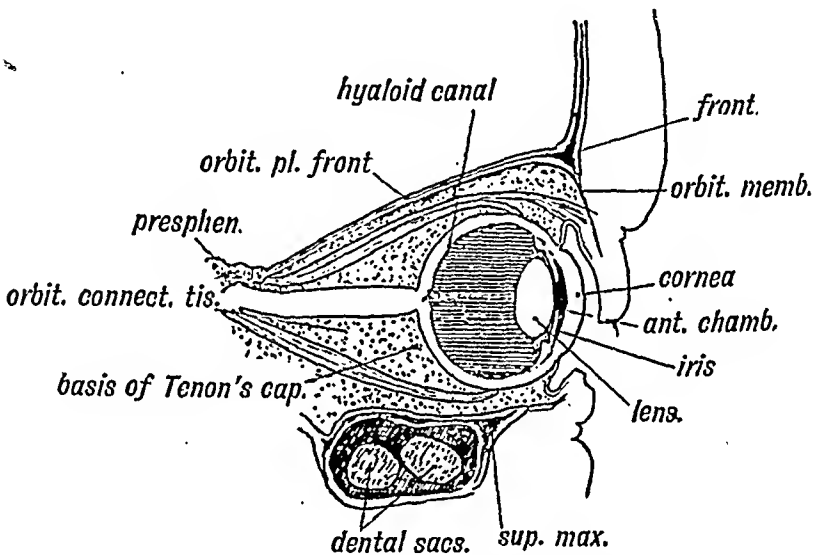
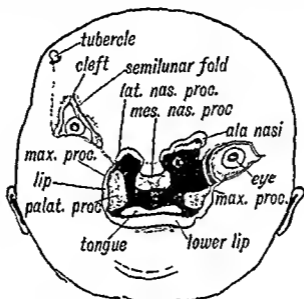


FIG. 260. Section of the Eye and Orbit at birth.

serving them as the pia mater does the brain. Within this vascular tunic certain unstriated muscles are developed. There is, first, the ciliary or focusing muscle, made up of circular as well as of radial fibres. It is developed in the mesoderm between the margin of the optic cup and the sclerotic during the 4th and 5th months, the circular being differentiated before the radial. Secondly, two unstriated muscles arise within the iris, one to act as a sphincter, the other as a dilator. These are remarkable in that they are developed directly from neurectoderm, being separated during the 4th month from that part of the optic cup which forms the deep stratum of the iris (Fig. 251). The only other muscles which arise from ectoderm are the arrectores pilorum.

The *sclerotic*, derived from the outer mesodermal envelope of the optic cup, is continuous in front with the cornea; behind, with the sheath of the optic nerve and dura mater. In some vertebrates, but not in mammals, plates of bone are developed in the anterior half of the sclerotic,

nasal, frontal process of maxilla, lachrymal and lateral mass of the ethmoid, are formed. The optic nerve enters the orbit between the orbito- and presphenoids, both of which help to form the orbit. The orbital surface of the great wing is formed at a later period in a membranous basis (see p. 220). The *orbital plate* of the malar cuts the orbit off from the temporal fossa; it is developed in higher primates only. The nasal duct is formed between the maxillary and nasal processes (Figs. 233 and 263). In lower primates and mammals generally the hamular process of the lachrymal appears on the margin of the orbit; the *pars facialis lachrymalis* is sometimes seen in the human skull



(Fig. 241). Mention has been made of the division of the orbital region of the primitive skull (Fig. 163) into orbital and temporal parts during the evolution of the temporo-mandibular joint (see p. 209). The division is effected by the formation of a lateral wall to the mammalian orbit; the lateral wall of the orbit should be regarded as part of a bony scaffolding to give attachment to muscles of mastication.

Eyelids.—The eyes lie naked in the head of the human embryo, like those of a fish, until the 7th week, when eyelids begin to form. They arise as folds of the ectoderm above and below the superficial parts of the eyeball. Mesoderm grows into the folds and forms the tarsal plates. The upper eyelid is developed from the same tissues as form the forehead, the lower from the visceral mesoderm of the maxillary process. In the 9th week the upper and lower eyelids meet and adhere, and remain

adults is usually about 68° . The forward swing of the eyes is an adaptation to binocular vision and is correlated with an extension in the development of mesodermal structures behind and lateral to the orbits (Fig. 261, *B*). These structures form the outer wall of the orbit and the mass of muscles concerned in mastication.

Growth of the Eyeball.—Up to this point we have been concerned with the assembling of the developmental parts of the eye. We must note now certain important changes which take place after birth. At birth the eye is relatively large, its diameter (17–18 mm.) being three-fourths of the adult diameter (24 mm.). In rate and precocity of growth it is comparable to the brain. Growth of the eyeball during childhood may assume a pathological character, the eye becoming unduly elongated,

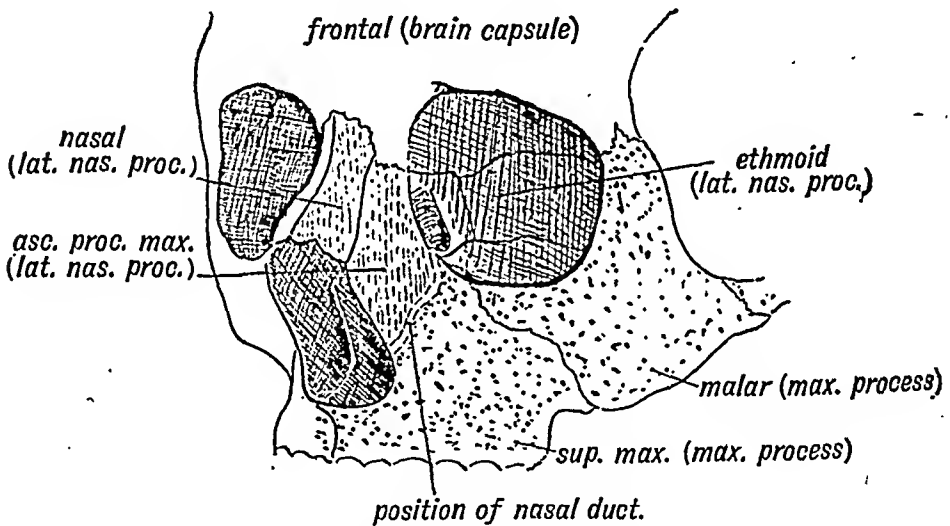


FIG. 262. The Origin of the Bones entering into the Formation of the Orbit. The ascending process of the maxilla, although lying in lateral nasal territory, is ossified as a direct extension from the body of the maxilla.

thus giving rise to *Myopia* [18]. The macula lutea and fovea centralis reach their full development about 4 months after birth [19]. A child born at the end of the 7th month is sensitive to light and darkness; appreciation of form comes towards the end of the 1st year; while colours are not recognized until the 2nd or 3rd years—or in some cases the colour sense is not developed. The colours at the opposite ends of the spectrum (red-violet) are the first to be recognized (Edridge Green).

Formation of the Orbit (Fig. 262).—The orbit is formed (i) above by the capsule of the fore-brain in which the frontal bone is developed, (ii) externally and below by the visceral mesoderm of the maxillary process (Fig. 261, *B*). In the maxillary process the malar bone and superior maxilla (except the ascending nasal process) are developed. (iii) The inner wall is formed by the lateral nasal process, in which the

The *Lochrymal Gland* arises at the beginning of the 3rd month as a number of ectodermal buds which spring from the fornix of the conjunctiva beneath the upper lid, and grow into the tissue of the outer and upper segment of the orbit (Fig. 266). The outer buds form the orbital part of the gland; the more internal buds form the palpebral part [21]. Smaller lachrymal glands may occasionally be found at the outer angle of the eye, which is the position occupied by the lachrymal glands of birds and reptiles (Wiedersheim). The lachrymal canaliculi and sac and nasal duct are developed out of solid epithelial cords enclosed between the maxillary and lateral nasal processes (see p. 291). The canaliculi are formed during the 3rd month as sprouts from the upper end of the solid rod of epithelium representing the nasal duct. While the bud of the upper canaliculus opens at the inner end of the upper lid

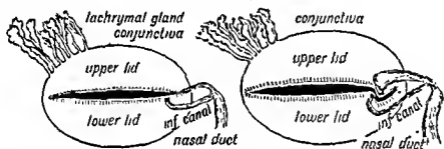


FIG. 266.

- A. Showing the Termination of the Lower Lachrymal Canaliculus some distance from the Mesial End of the Lower Eyelid, in a foetus 2 months old. The tubular outgrowths of the lachrymal gland are also shown.
- B. The Mesial Extremity of the Lower Eyelid cut off to form the Caruncula. The lachrymal outgrowths are now more complex in structure. From a foetus in 4th month of development. (After Ask)

(Fig. 266, A), the inferior canaliculus extends some way along the lower lid before it comes to the surface (Ask). It may form a secondary communication nearer the inner angle of the eye, thus giving rise to a congenital lachrymal fistula. With the formation of the lachrymal canaliculus, part of the lower eyelid is cut off and forms the caruncula (Fig. 266, A and B). The nasal duct was evolved when vertebrates abandoned water for life on land. Thus arise the various parts of the system concerned in bathing, cleansing and draining the front of the eye. In man this system serves an emotional as well as a utilitarian purpose.

Ocular Muscles.—In Fig. 180 are represented the various parts of a primitive cranial segment. In such a segment the upper part (head cavity) gives origin to a "muscle plate"—as happens also in body segments. From the head cavities of the first three visceral processes arise the muscles of the eyeball [22]. These muscles become

adherent until the 7th month is entered. In rabbits, mice, kittens and puppies the lids are still closed at birth. The upper eyelid is developed in two parts—outer and inner; occasionally a notch remains on the margin, and marks the point at which the two parts unite (Fig. 263). The upper end of the plica semilunaris is attached in the embryo at the position of the notch. The ectoderm on the deep surface of the lids retains a columnar shape, and forms the palpebral conjunctiva. It is continuous with the ectodermal stratum of the cornea. From the ectoderm between the adherent edges of the lids, buds grow during the 4th and 5th months, and form the eyelashes, Meibomian and other glands, in the same manner as hairs and sweat glands, are developed. The Meibomian glands represent modified sebaceous glands, but the hair or cilia from which they primarily arose have vanished. The curious epicanthic fold is shown in Fig. 264. It is represented in all races

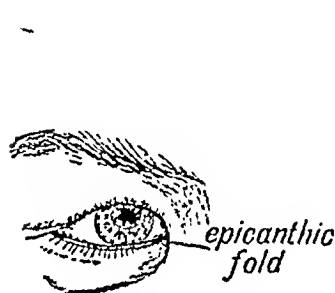


FIG. 264.

FIG. 264. Epicanthic or Mongolian fold. (After Meckel.)

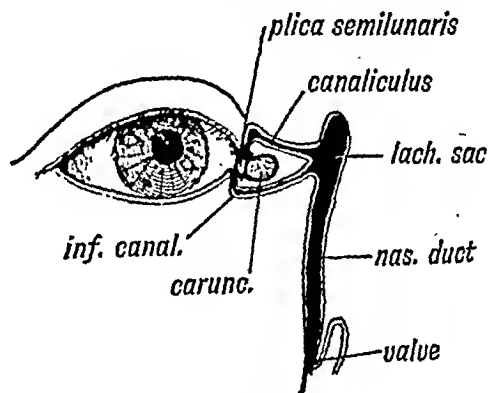


FIG. 265.

FIG. 265. Diagram of the Plica Semilunaris and Lachrymal Canaliculi.

during foetal life. Towards the end of the 2nd month the eyelids are invaded by myoblasts—muscle cells—derived from the 2nd or hyoid visceral arch. The orbicularis palpebrarum which thus arises is supplied by the facial nerve, the nerve of the hyoid arch.

The *plica semilunaris* (Fig. 265), a fold of conjunctiva in the inner canthus of the eye, has hitherto been regarded as a vestige of the 3rd eyelid (*membrana nictitans*), which is fully developed in birds and reptiles. In the snake's eye Mayou found that this membrane formed what is commonly called the anterior lamina of the cornea; it is the epithelium of this membrane which desquamates and renders the animal temporarily blind. The *plica semilunaris* is relatively large in the human foetus, reaching its maximum development in the 5th month. It is well seen in the cat, partially crossing the cornea as the lids are shut [20]. The lachrymal papillae in man rub in the grooves at the outer and inner margins of the fold.

ciliary, and its nerve, the oculomotor, both also derivatives of the 1st segment [25]. Mention has been made of the origin of the retractor muscle with the external rectus from the 3rd segment.

Development of the Nerve Centres concerned with Sight.—Four parts of the brain are concerned with vision. They are: (i) Optic tracts. (ii) Basal centres in the optic thalamus (lateral geniculate bodies) and in the tectum (superior colliculus). (iii) Optic radiations. (iv) Occipital lobes—in part at least.

(i) The *optic tracts* are made up of fibres developed from the ganglionic cells of the retina and also in part of efferent fibres developed from cells of the basal ganglia in which the optic tracts are seen to terminate. The fibres grow in by the optic stalk, those from the nasal fields of the retina decussating in the floor of the 3rd ventricle between the origins of the optic vesicles, thus forming the chiasma. The optic fibres grow backwards on the surface of the thalamencephalon (see Fig. 268) and on the optic thalamus to reach the lateral or external geniculate body. The majority of the fibres of the optic tract end in this geniculate centre. The fibres from the macula are almost as numerous as from the rest of the retina. The optic fibres on reaching the geniculate cortex take up definite positions—the macular fibres occupying one area, the peripheral fibres adjacent areas (Fig. 272). In brief, it may be said that the representation of the retina in the lateral geniculate bodies is strictly anatomical. The crossed and uncrossed fibres from the corresponding quadrants of the retina find their appointed places in the geniculatae, those from the upper quadrants of the retina ending in the deeper or mesial aspects of the body, while those from the lower quadrants end in the more superficial or lateral strata of that body.

(ii) *Basal Centres.*—*Corpora quadrigemina.*—In a number of instances the human embryonic condition resembles the adult condition of lower vertebrates. A good example is seen in the corpora quadrigemina or tectum. The human foetus at the end of the 2nd month (Fig. 268) shows the corpora quadrigemina represented by a prominent thickening in the roof of the cavity of the mid-brain, which forms subsequently the aqueduct of Sylvius. The thickening is divided into lateral halves by a median sulcus, each half being nearly as large as the cerebral vesicle of that period. In Fig. 269 is shown the condition in an adult lizard; there is one body on each side—the *optic lobes*, tectum or corpora bigemina. As the human foetus grows older, each lateral lobe becomes divided into an upper and lower colliculus by the formation of a transverse groove, the upper and lower pairs of the corpora quadrigemina being thus formed. The upper pair are connected with sight in all vertebrates, but in the higher primates, including man [26], the number

differentiated towards the end of the 2nd month. The levator palpebrae arises as a delamination from the superior rectus in the 3rd month. The muscle plate of the premandibular—usually called the 1st—segment forms the muscles supplied by the IIIrd cranial nerve, which is the motor nerve of that segment. The mesencephalon (*crura cerebri*) contains the corresponding part of the neural tube. The ciliary muscle and sphincter of the iris also belong to this segment, and are supplied by the IIIrd nerve. The muscle plate of the mandibular, usually named the 2nd head segment, produces the superior oblique. The dorsal decussation and anomalous position of the IVth nerves have, as yet, received no satisfactory explanation [23]. The muscle plate of the hyoid or 3rd cephalic segment gives rise to the external rectus; the VIth

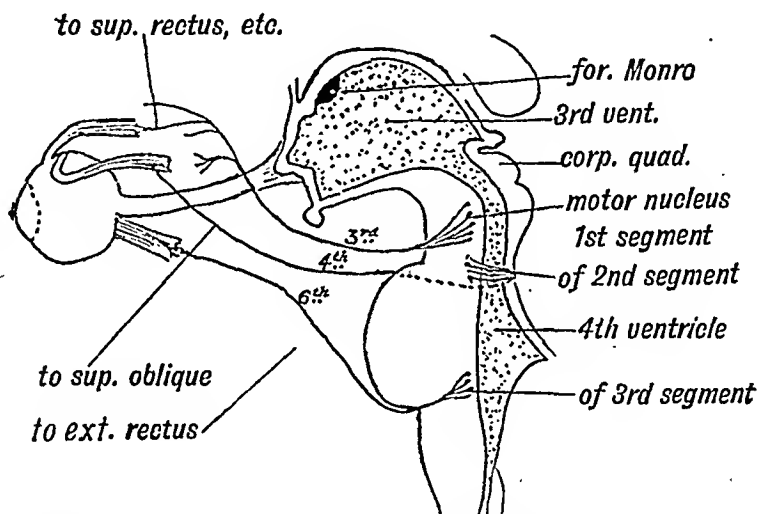


FIG. 267. Diagram of the Motor Nerves of the Muscles of the Eye derived from the 1st, 2nd, and 3rd cephalic segments.

nerve is the nerve for the somatic musculature of the segment, the VIIth supplying the splanchnic muscles of that segment.

The sensory nerves of these three segments are fused together in the three divisions of the Vth nerve. The ciliary ganglion is the splanchnic (sympathetic) ganglion of the premandibular segment [24]. The nerves for the retractor muscle, the non-striated muscle of the upper eyelid and the dilator fibres of the iris issue from the upper three dorsal segments of the spinal cord and reach the eye by the cervical sympathetic chain and cavernous plexus. The nerve fibres for the orbicularis palpebrarum pass out with the facial, but their cells of origin receive collaterals from each pyramidal tract. The ophthalmic division of the Vth represents the sensory somatic nerve of the segment to which the IIIrd nerve belongs; hence the reflection of pain along this nerve (frontal headache) in disorders of accommodation, the muscle of accommodation being the

colliculi are vestigial, but in compensation, the inferior are well developed as they are connected with the sense of hearing, which is very acute in that animal.

The lateral geniculate body is part of the great sensory transmitting station, the optic thalamus. It will be remembered (p. 183) that the thalamus in its evolution and development moves at the same pace as the cerebral cortex. In reptiles, stages in the transference of sensory terminations from the mid-brain to the thalamus are to be seen. This transference was continued in the mammalian stock, reaching its highest points in the anthropoid and particularly in the human brain. Prof. Le Gros Clark [26] found that the lateral geniculate body is developed from the ventro-lateral nucleus of the thalamus, the nucleus which receives all the sensory tracts of the body, save those from the olfactory bulbs. He observed, too, that there is added to its ventral aspect a subsidiary part, derived from the older subthalamus. In the 3rd month the recipient cells of the main nucleus become arranged in six tiers or strata [27] between which the fibres of the optic tract end in the orderly manner already mentioned (p. 315).

The *optic radiations* connect the geniculate centres with the striate cortex of the occipital lobes, and *vice versa*. The fibres join the posterior part of the internal capsule, and pass under and round the posterior horn of the lateral ventricle to end in the cortex of the calcarine fissure and neighbourhood. The granular stratum (IV) of the cortex in which the optic radiations terminate is divided by a narrow white stratum, the *line of Gennari*, into a superficial and deep layer. In reptiles, as already said, the optic tracts end chiefly in the mid-brain; there are no optic radiations. These begin to appear in the lowest mammals, connecting the lateral geniculate centres with the cortex of brain and thus bringing vision into the field of consciousness. In man and higher primates the transference to the cortex has become almost complete. Even in their distribution in the occipital cortex the impulses from the retina retain orderly pathways; the quadrants of the retina have corresponding fields in the occipital cortex on the upper and lower lips of the calcarine fissure. The peripheral fields of the retina have, as has just been mentioned, their main representation in the main calcarine fissure, while the macula finds its visual field in the cortex around the retrocalcarine and lateral calcarine sulci (Fig. 272). The blood supply to all parts connected with vision is remarkably constant [28].

The occipital lobe and calcarine fissure.—A mesial view of the 5th-month foetal brain is shown in Fig. 270, *A*. The occipital lobe is already well formed; its inner aspect shows the calcarine and parieto-occipital fissures. A section across the occipital lobe is shown in Fig. 270, *B*;

of fibres terminating in the superior colliculi is greatly reduced. Indeed, those which do terminate there convey stimuli which are ultimately

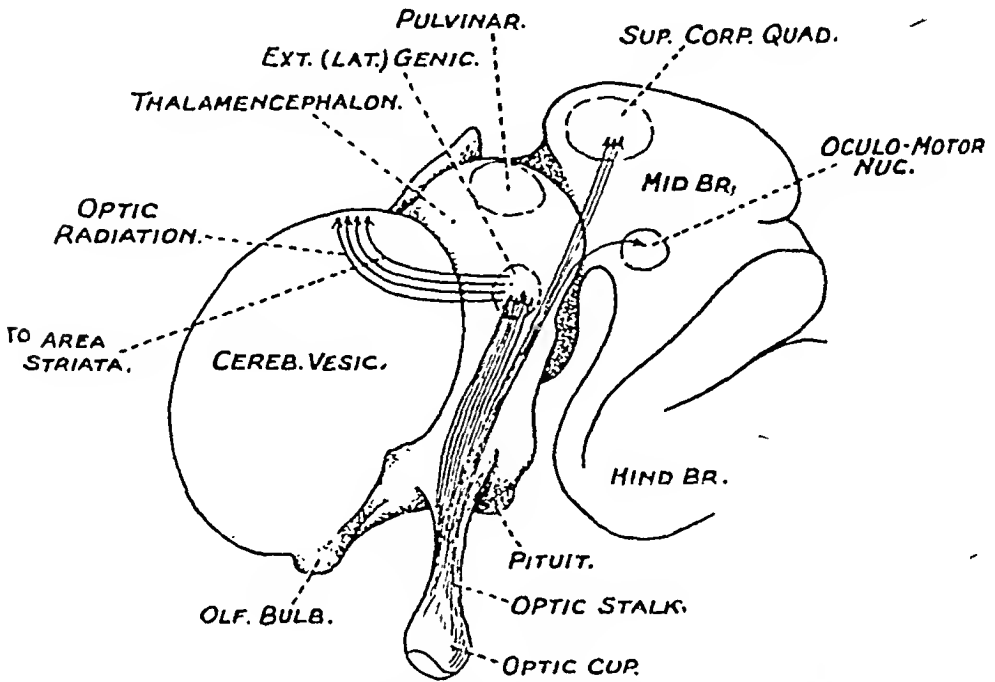


FIG. 268. Diagram of the Foetal Brain at the end of the 2nd month, showing the position in which the optic tracts are developed.

concerned in regulating the size of the pupil. In the reptilian brain, on the other hand, nearly all the optic fibres end in the mid-brain, few terminating in the geniculate body. The mid-brain is the sight brain

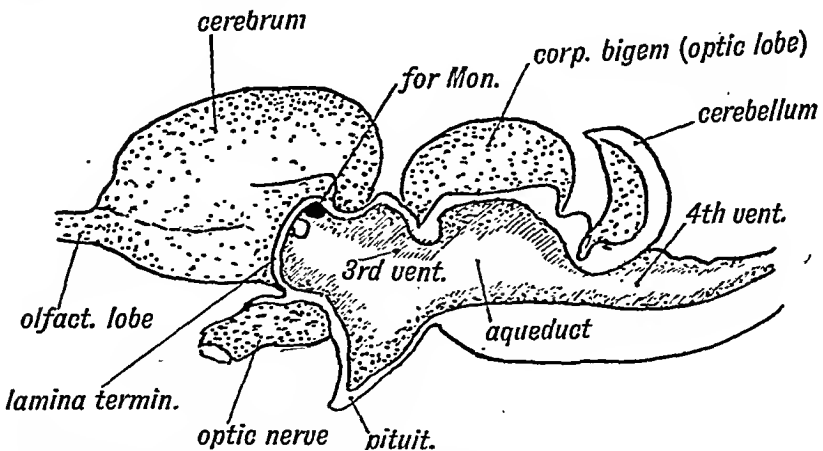


FIG. 269. Mesial section of the Brain of a Lizard, showing the resemblance to the human foetal brain, especially in the development of the corpora bigemina.

and chief executive centre of the reptile. In four-footed mammals, although the geniculate centres rise in importance, yet more than half the optic fibres still pass to the mid-brain. In the mole the superior

back to overlap the cerebellum. The striate or visuo-sensory area of the human brain is not larger than that of the anthropoid ape, but the association or visuo-psychic area is infinitely more extensive. "Thus, we can take it that the superiority of the human over the ape's brain as a psychical organ must be the result mainly of the higher development of the association or peristriate areas" (Elliot-Smith). With the development of association areas in front of the occipital cortex in the human brain, the striate area tends to be pushed towards the mesial aspect of the cerebral hemispheres.

The *angular gyrus* is linked to the occipital lobe by association fibres. It is only indirectly connected with vision. There is clinical evidence to suggest that its cortex is concerned in the interpretation of what is seen. This gyrus is developed round the posterior end of the 1st temporal or parallel fissure (Fig. 151). It is part of the wall of the cerebral vesicle. The first temporal or parallel fissure appears during the 6th month and

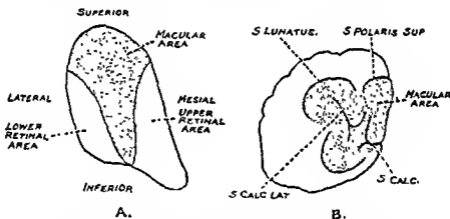


FIG. 272.

A The Areas of Termination of Retinal Fibres in the Lateral Optic Tectum. (Brouwer)

B, The "Macular Area" of the Occipital Lobe. (Elliot-Smith.)
s. calc. lat., lateral calcarine sulcus

is one of the primary fissures. It is found in the brains of all primates except the lowest [29].

It will thus be seen that three parts of the neural tube have become modified to serve the function of sight: (i) The optic vesicle, an out-growth from the fore-brain (thalamencephalon). (ii) The occipital region of the cerebral vesicle, which receives fibres projected from the geniculate nuclei. (iii) The walls of the 3rd ventricle (thalamencephalon) and mid-brain (mesencephalon). The tunics of the eye are extensions of the embryological coverings of the brain, the retina being an extension of the brain itself. The choroid coat springs from the same layer as forms the pia mater and arachnoid. The sclerotic is a

the posterior horn is large; the calcarine fissure indents its inner wall, giving rise to the *calcar avis* or hippocampus minor, a feature which is seen in the brains of nearly all mammals (Elliot-Smith).

The *calcarine* is one of the first fissures to be formed on the brain;

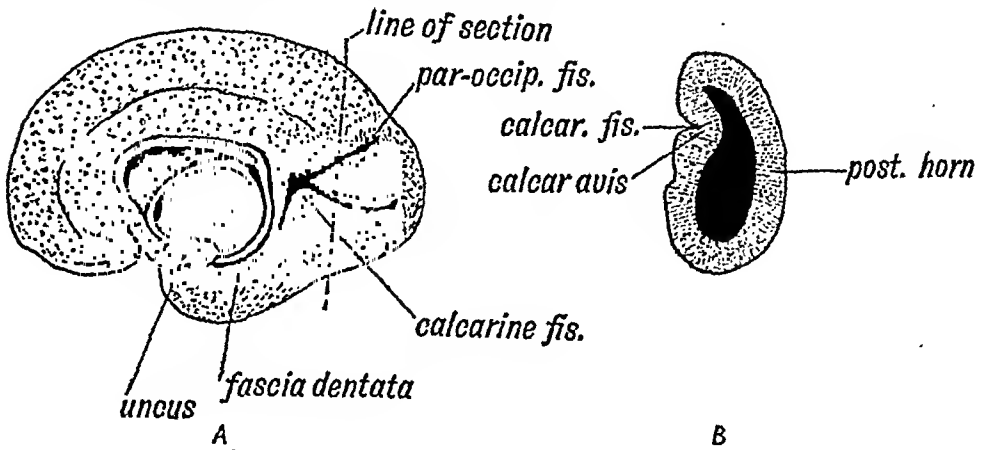


FIG. 270.

A. View of the Mesial Surface of the Brain in the 5th month.

B. Section of the Occipital Lobe at the position marked in A.

it appears early in the 5th month. This and the hippocampal depression, which is connected with the sense of smell, are the two fissures most commonly present in the mammalian brain. The posterior part of the calcarine fissure is a later formation, and is distinguished as the retro-

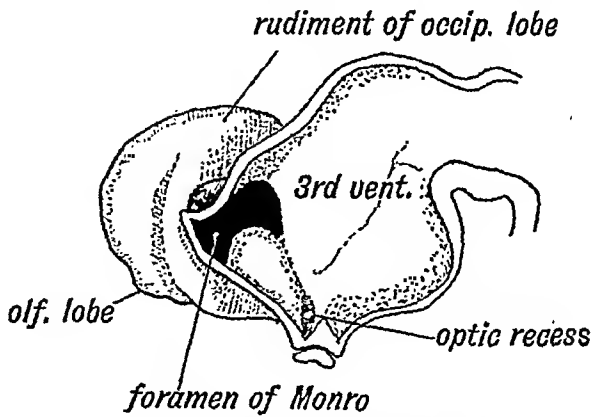


FIG. 271.—Mesial section of the Brain in the 5th week, showing the rudiment of occipital lobe. (After His.)

calcarine (see Fig. 157, p. 198). In Fig. 271 the condition of the occipital lobe in the 5th week is shown. The lateral ventricle is as yet undifferentiated into horns, and only the rudiment of the occipital lobe is present. This lobe develops as a backward growth of the cerebral vesicle, the posterior horn being produced as a diverticulum of the cavity of the vesicle. By the 5th month the occipital lobe has reached far enough

[23] An explanation of the dorsal origin of the trochlear nerve is likely to be found amongst pre-vertebrate forms. For an explanation of its decussation, see Shafik, Abd-el-Malak, *Jour. Anat.*, 1938, 72, 522; see also Frazer's *Manual of Embryology*, pp. 160, 197.

[24] The late Prof. Woollard found that the nerves to the ocular muscles have two forms of termination, by end plates (motor), and by branched endings (sensory): see *Jour. Anat.*, 1931, 65, 215; Hines, M., *Amer. Jour. Anat.*, 1931, 47, 1; Tarkhan, A. A., *Jour. Anat.*, 1934, 68, 293.

[25] For central connections of the Vth nerve, see Stopford, Sir John, *Jour. Anat.*, 1925, 59, 120; Carmichael and Woollard, *Brain*, 1933, 56, 109.

[26] For recent work on lateral geniculates, see Clark, W. E. Le Gros, *Brain*, 1932, 55, 406; *Proc. Roy. Soc.*, 1934, 114 (B), 291; *Jour. Anat.*, 1941, 75, 419; *ibid.*, 1942, 76, 131 (in S. American monkeys); Glees and Clark, *ibid.*, 1941, 75, 295; Mackenzie, Ivy, *Jour. Path. Bact.*, 1934, 39, 113; Elliot-Smith, Sir G., *Nature*, 1930, 125, 820.

[27] For connections of lateral geniculates, see Brouwer, B., *Anatomical and Clinical Studies of the Central Nervous System*, 1927; Glees and Clark, see reference in preceding note.

[28] For blood-supply of parts connected with vision, see Abbie, A. A., *Med. Jour. Australia*, 1938, p. 199; see also references to Shellshear, J., note [26], Chapter XI.

[29] For morphology of occipital convolutions, see references, note [19], Chapter XI.

prolongation of the primitive cerebral capsule, in which the skull bones are formed. The optic vesicle carries with it a prolongation of the arteries and veins of the fore-brain. Part of the optic vesicle is transformed into a secretory epithelium over the ciliary processes in the same way as the wall of the neural tube becomes a covering for the choroidal villi of the brain.

NOTES AND REFERENCES

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[2] For more detailed account of the development of the eye, see Mann, Ida, *The Development of the Human Eye*, 1928; *Developmental Abnormalities of the Eye*, 1937; Frazer, J. E., *Manual of Embryology*, 1940. For development of lens, Bleehschmidt, E., *Zeitsch. Anat. Entwickl.*, 1937, 107, 508.

[3] For induction of the lens, see references, note [3], Chapter IV; Danchakoff, Vera, *Contrib. Emb.*, 1926, 17, 63; Strangeways and Fell, *Proc. Roy. Soc.*, 1926, 150 (B), 273; Needham, J., *Biochemistry and Morphogenesis*, 1942.

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[5] References to literature on "organizers" are given in notes [1], [6], Chapter IV.

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[7] Cameron, J., *Jour. Anat.*, 1905, 39, 135.

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[10] Mann, Ida, see under note [1].

[11] Strangeways and Fell, see note [3].

[12] Mann, Ida, see under note [2]; Meadley, J. C., *Brit. Jour. Physiol. Optics*, 1936, 10, 193.

[13] *Anat. Hefte*, 1915, 52, 195.

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[18] Keith, Sir A., *Brit. Jour. Physiol. Optics*, 1925, 1, 369.

[19] Mann, Ida, see under note [2].

[20] Stibbe, E. P., *Jour. Anat.*, 1928, 62, 159; Loewenthal, N., *Archiv. d'Anat.*, 1932, 15, 1.

[21] Ask, F., *Anat. Hefte*, 1910, 40, 489; *ibid.*, 36, 189; Moeller-Holst, G., *Archiv. Anat. Entwickl.*, 1933, 31, 105.

[22] For evolution and development of the ocular muscles, see Edgeworth, F. H., *Jour. Anat.*, 1930, 64, 369; *The Cranial Muscles of Vertebrates*, 1935; Mann, Ida, see under note [2].

rinth. Some of its lining cells are differentiated into ciliated sensory epithelium. The otocyst appears remarkably early in the human embryo, the plaque being recognizable at the beginning of the 4th week, when only five or six body segments have become demarcated.

(ii) A ganglion, which is also differentiated at a very early period from the projecting angle of the hind-brain, representing a forward continuation of the neural crest (Fig. 273). The neural cells so separated become the ganglia of the VIIth and VIIIth nerves—the mass belonging to the VIIIth migrating towards and becoming closely applied to the otocyst.

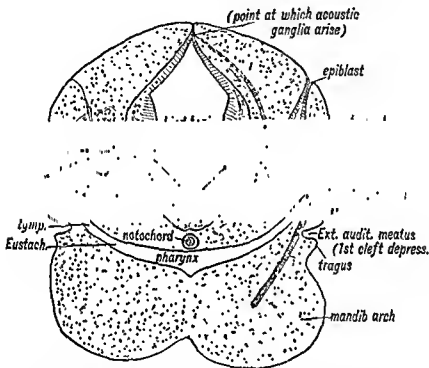


FIG. 273. Diagrammatic section through the Cephalic Region of an Embryo, showing the origin of the constituent elements of the Auditory System

The nerve cells so applied form the cochlear and vestibular ganglia. Each cell sends out two processes, one to become connected with the epithelium of the otocyst, the other to end in groups of nerve cells in the floor of the hind-brain, their collective fibres forming the vestibular and auditory divisions of the VIIIth nerve. The development of the auditory nerve thus resembles that of the posterior or sensory root of a spinal nerve.

(iii) The otocyst (membranous labyrinth) becomes surrounded by a capsule of cartilage—the *periotic capsule*. This ossifies from several centres, and forms the bony labyrinth and petro-mastoid.

(iv) The Eustachian tube, the tympanum and the antrum of the

CHAPTER XVII

THE ORGAN OF HEARING

The Nature of the Labyrinth.—It often happens, when we seek to interpret the developmental changes which give rise to an organ or system of the human body, that a reference to the condition seen in certain groups of fishes—especially those belonging to the shark kind, selachians—gives us great assistance. This is true as regards the organ of hearing. In a shark or ray every part of the internal ear—the labyrinth with its semicircular canals—is already evolved with the exception of one part, the canal of the cochlea; it is represented by a mere rudiment. The labyrinth of the shark is not an organ of hearing, for it is generally admitted that fishes are insensitive to sound waves, but for the balancing or orientation of the body. Most men who have investigated the nature of the labyrinth of fishes agree that it represents a specialization of one of a series of superficial sense organs set on the sides of fishes—the organs of the lateral line—these also being connected with the functions of balancing and movement. Hence we find that the labyrinth begins as a pocket-like invagination of the ectodermal covering in the head region. The essential element of the labyrinth is its ciliated epithelium; movements of the cilia, produced in various ways, give rise to stimuli which pass by the VIIIth nerve to the hind-brain. The auditory or cochlear part of the labyrinth appeared when the land-forms of vertebrates were evolved. In vertebrates above fishes the rudiment of the cochlea begins to be differentiated and an apparatus for converting sound waves into mechanical waves in the labyrinth is evolved. A vibrating drum is established in the site of the first of the pharyngeal or visceral clefts. We must also suppose that in the reptilian type from which mammals arose the mammalian form of mandible was already evolved, for it is from remains of the primitive cartilaginous skeleton of the lower jaw that the malleus and incus are differentiated in the human and mammalian embryo [1].

Structures which form the Organ of Hearing.—In Fig. 273 is shown diagrammatically the derivation of the five elements which unite together to make up the organ of hearing. The five elements are:

(i) The *otocyst*—an area or plaque of ectoderm on the head of the embryo above the first visceral cleft which becomes invaginated in a saccular form, to become the epithelial lining of the membranous laby-

rinth. Some of its lining cells are differentiated into ciliated sensory epithelium. The otocyst appears remarkably early in the human embryo, the plaque being recognizable at the beginning of the 4th week, when only five or six body segments have become demarcated.

(ii) A *ganglion*, which is also differentiated at a very early period from the projecting angle of the hind-brain, representing a forward continuation of the neural crest (Fig. 273). The neural cells so separated become the ganglia of the VIIth and VIIIth nerves—the mass belonging to the VIIIth migrating towards and becoming closely applied to the otocyst.

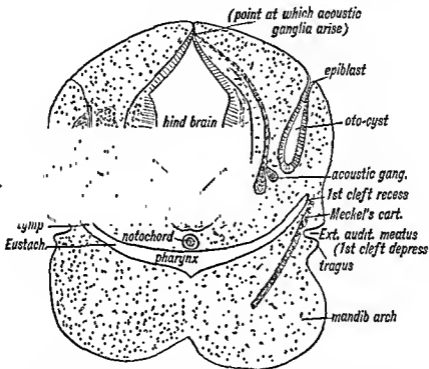


FIG. 273. Diagrammatic section through the Cephalic Region of an Embryo, showing the origin of the constituent elements of the Auditory System.

The nerve cells so applied form the cochlear and vestibular ganglia. Each cell sends out two processes, one to become connected with the epithelium of the otocyst, the other to end in groups of nerve cells in the floor of the hind-brain, their collective fibres forming the vestibular and auditory divisions of the VIIIth nerve. The development of the auditory nerve thus resembles that of the posterior or sensory root of a spinal nerve.

(iii) The otocyst (membranous labyrinth) becomes surrounded by a capsule of cartilage—the *periotic capsule*. This ossifies from several centres, and forms the bony labyrinth and petro-mastoid.

(iv) The Eustachian tube, the tympanum and the antrum of the

mastoid arise in connection with the pharyngeal pocket between the mandibular and hyoid arches ; the corresponding external cleft depression forms the point of origin for the external auditory meatus ; while out of the tissue between the internal pocket and external cleft, representing in position a "cleft-membrane," is formed the *membrana tympani*.

(v) The *hyomandibular cartilage* (Fig. 208), which served primarily to bind the cartilages of the maxillary process, mandibular and hyoid arches to the base of the skull, becomes the stapes. The incus and

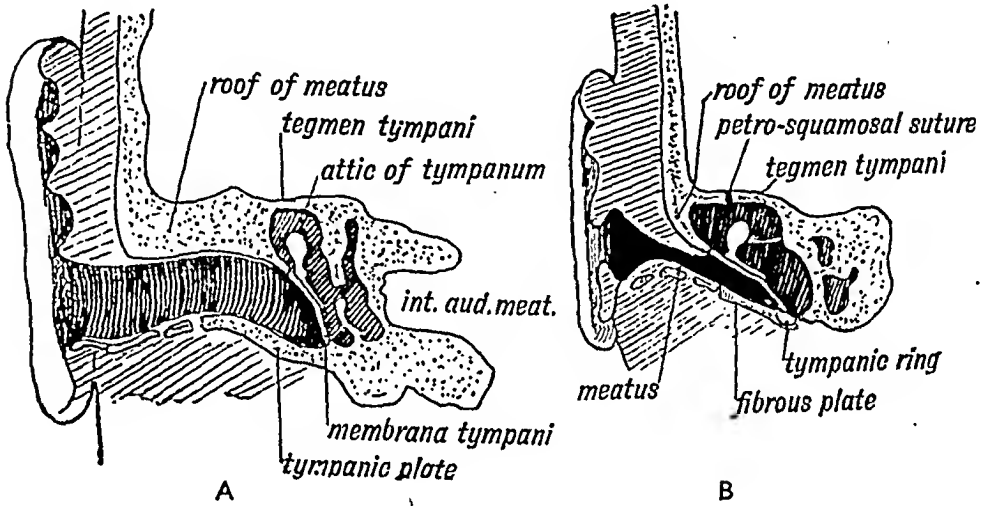


FIG. 274.

A. A section of the External Auditory Meatus of the Adult.

B. A section of the External Auditory Meatus at Birth. (After Symington.)

malleus arise from the upper end of the mandibular (Meckel's) bar of cartilage (Figs. 209, 213).

In fishes the auditory apparatus is composed of the three elements named first, viz.—the *otocyst*, *ganglion* and *periotic capsule*. In amphibians, reptiles and birds a *membrana tympani* is developed, which is connected with the inner ear by an unjointed derivative of the *hyomandibular cartilage*, the *columella*. In mammals a *tympanic cavity*, *external auditory meatus*, and *auditory ossicles* appear.

External Auditory Meatus.—A section along the external meatus of a newly born child shows that it is divided by a constriction into outer and inner parts (Fig. 274, B). The outer part is derived directly from the first cleft depression ; the inner part arises during the 2nd and 3rd months by a solid ingrowth of epithelium, which, commencing from the cleft depression or pit, grows inwards until it comes in contact with the handle of the malleus, when it expands to form the fundus of the meatus (Figs. 275, 281). During the 7th month the deeper part of the meatus

and outer aspect of the drum are formed by a breaking down of the central, and therefore older, cells of this ingrowth. Cartilage surrounds the part of the meatus derived from the cleft; the floor of the deeper part is formed at birth by a fibrous plate continuous with the tympanic ring. In the adult the tympanic ring has grown outwards in the fibrous tissue, as we have already seen (p. 260), to form the tympanic plate and the inner two-thirds of the meatal floor. The squamous part of the temporal, which is developed in its roof, also grows outwards, and forms a thick, horizontal plate in the inner two-thirds of the meatal roof (Fig. 274, *A* and *B*). Over the roof lies the 3rd temporal convolution.

The meatus is supplied in front by the nerve of the mandibular arch (auriculo-temporal branch) and also by a branch from the nerve of the hyoid arch—the facial. Why the vagus should supply it with a branch (Arnold's nerve) is obscure. In fishes a branch of the vagus passes back-

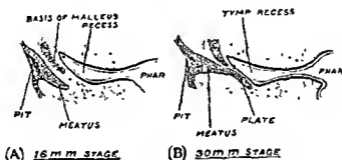


FIG 275. Showing the growth of the External Meatal Plug and its relationship to the tympanic recess of the pharynx. (Prof. Frazer.)

wards beneath the skin on each side and supplies the sense organs of the lateral line. Many regard the auricular branch of the vagus as a vestige in the mammal of such a branch.

In the newly horn child the membrana tympani is so obliquely set that its outer surface is almost in contact with the meatal floor (Figs. 274, *B*, 281). The membrana tympani, like the internal ear, is full-size at birth. Its obliquity allows it to be the more easily accommodated in the child's head. With the development in length of the meatus, it becomes more vertical in position. The deeper part of the meatus may fail to form or the whole cleft may remain closed. In such cases the labyrinth is usually normally formed and hearing may be quite good [2].

External Ear.—Six elevations or tubercles appear on the mandibular and hyoid arches round the uppermost part of the 1st cleft depression during the 6th week and form the basis of the external ear (Figs. 276 and 277). Three of these tubercles appear to grow from the mandibular arch and form the tragus (*a*), crus of the helix (*b*), and ascending helix (*c*),

mastoid arise in connection with the pharyngeal pocket between the mandibular and hyoid arches; the corresponding external cleft depression forms the point of origin for the external auditory meatus; while out of the tissue between the internal pocket and external cleft, representing in position a "cleft-membrane," is formed the membrana tympani.

(v) The *hyomandibular cartilage* (Fig. 208), which served primarily to bind the cartilages of the maxillary process, mandibular and hyoid arches to the base of the skull, becomes the stapes. The incus and

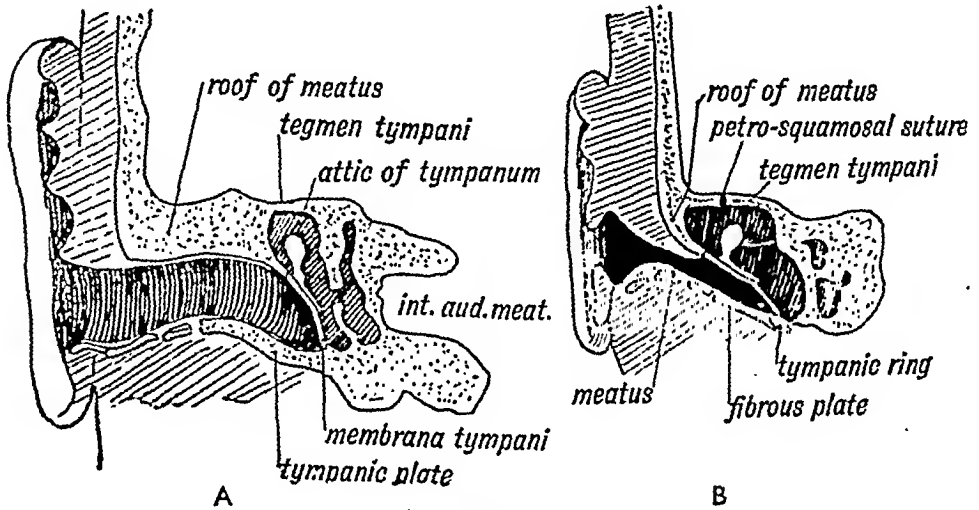


FIG. 274.

A. A section of the External Auditory Meatus of the Adult.

B. A section of the External Auditory Meatus at Birth. (After Symington.)

malleus arise from the upper end of the mandibular (Meckel's) bar of cartilage (Figs. 209, 213).

In fishes the auditory apparatus is composed of the three elements named first, viz.—the otocyst, ganglion and periotic capsule. In amphibians, reptiles and birds a membrana tympani is developed, which is connected with the inner ear by an unjointed derivative of the hyomandibular cartilage, the *columella*. In mammals a tympanic cavity, external auditory meatus, and auditory ossicles appear.

External Auditory Meatus.—A section along the external meatus of a newly born child shows that it is divided by a constriction into outer and inner parts (Fig. 274, B). The outer part is derived directly from the first cleft depression; the inner part arises during the 2nd and 3rd months by a solid ingrowth of epithelium, which, commencing from the cleft depression or pit, grows inwards until it comes in contact with the handle of the malleus, when it expands to form the fundus of the meatus (Figs. 275, 281). During the 7th month the deeper part of the meatus

Muscles of the External Ear are derived from the platysma sheet and are supplied by the nerve of that sheet—the VIIth or facial. The part of the platysma which surrounds the external meatus and acts on the ear appears to have been the first of the facial muscles to be evolved. The ear muscles are not so reduced in man as in some other primates, such as the orang [3].

Eustachian Tube.—The Eustachian tube has usually been regarded as a derivative of the first of the inner cleft recesses—a diverticulum of the lining membrane of the primitive pharynx between the mandibular and hyoid arches. Prof. Frazer [6] made a thorough inquiry into its development, and found that its origin is more complicated than was supposed.

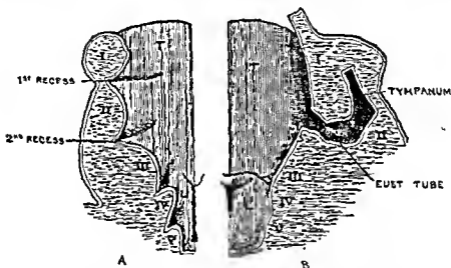


FIG. 278. Figures illustrating the Development of the Eustachian Tube and Tympanum. (After Prof. Frazer.)

- A* The Floor of the Pharynx of a Human Embryo 5 weeks old. The visceral arches (I, II, III, IV, V) are cut across and the inner cleft recesses indicated.
- B* The Floor of the Pharynx of a Human Foetus 7 weeks old, showing the origin of the Eustachian tube by an evagination of the pharynx opposite the 2nd or hyoid visceral arch. *T*, rudiments of tongue on floor of pharynx, *L*, larynx.

In Fig. 278, *A*, the left half of the floor of the pharynx of a human embryo, five weeks old, is represented. Between the 1st and 2nd and between the 2nd and 3rd arches the lining mucous membrane of the pharynx is seen to dip outwards and at first is actually in contact with the ectoderm; as yet there is no sign of Eustachian tube or of tympanum. In Fig. 278, *B*, the opposite half of the floor of a pharynx towards the end of the 2nd month of development is shown; the basis of the Eustachian tube and tympanum is now apparent as a wide recess between the 1st and 3rd arches, the hyoid arch having been thrust into the outer wall of the recess. The oblique fold forming the roof and posterior wall of the Eustachian tube is formed by the forward growth of the substance of

three from the hyoid to form horizontal helix (*d*), descending helix (*e*), antitragus (*f*) and the lobule, which is part of the antitragal elevation [3]. During the latter part of the 2nd month and first part of the 3rd, the pinna begins to assume its definite form. The tubercles of the crus helicis (*b*) and of the descending helix (*e*), which gives rise to the antihelix (*g*), send out processes that cross the upper part of the cleft and obliterate it, while the neighbouring tubercles fuse to form the definite parts of the ear. The helical margin of the ear is markedly raised and folded at the end of the 3rd month—a condition which may pass unchanged into adult age. The auricular tubercles may not fuse completely and thus leave fistulae between them. Such fistulae are commonly seen between the tragus and root of the helix, or between the antihelix and

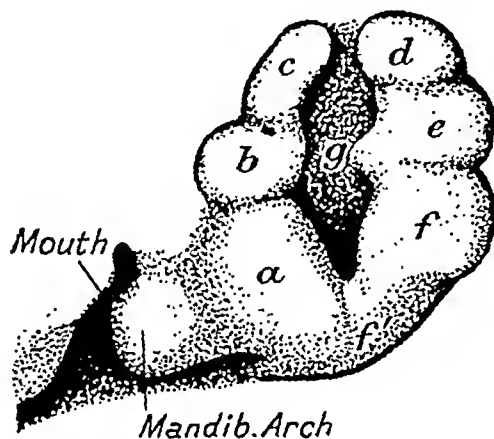


FIG. 276.

FIG. 276. The Tubercles which arise round the upper part of the First Visceral Groove to form the External Ear. (After Streeter.)

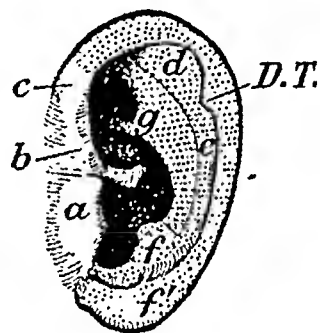


FIG. 277.

FIG. 277. Showing the parts of the Ear formed by each Tubercle. *a*, tragus; *b*, crus of helix; *c*, ascending helix; *d*, horizontal helix; *e*, descending helix; *f*, antitragus; *f'*, lobule; *g*, antihelix; *D.T.*, Darwin's tubercle.

the helix [4]. Only the tragus is supplied by the third division of the Vth (Wood-Jones), while the sensory fibres for the remaining parts come from the IInd cervical by the great auricular and small occipital nerves [3].

Darwin's Tubercle [5].—The human ear appears to be derived from a form in which the margin was pointed at the posterior superior angle, such as is seen in many of the lower forms of apes and mammals generally. With the retrogression of the posterior border or descending helix and increased development of the antihelix in the human ear, the posterior margin became infolded; hence the tip appears as a tubercle on the inturned margin or welt of the human ear (Fig. 277, *D.T.*). The small size and restricted mobility of the external ears of higher primates result from the free manner in which these animals can turn their heads in the direction of sounds.

tympanic recess, in which are represented both 1st and 2nd pharyngeal pockets, extends outwards and backwards, the gelatinous tissue is absorbed, so that, in the later months of development, the malleus and incus and developing stapes, with the chorda tympani, become surrounded by the endodermal lining of the recess and thus appear to lie within the cavity thus formed—the tympanum. The tympanic plate forms the floor of the tympanum, the membrana tympani and squamosal its outer wall, while the petro-mastoid forms its inner wall and roof (Fig. 280). The nerve of the 2nd arch—the facial—lies in its inner or mesial wall. Attached to this wall is a derivative of the hyoid arch—the stapes. That part of the tympanum which lies above the level of the membrana tympani is named the *attic*, and contains the head of the malleus and body of the incus (Fig. 274).

In carnivora and some other mammals the floor of the tympanum,

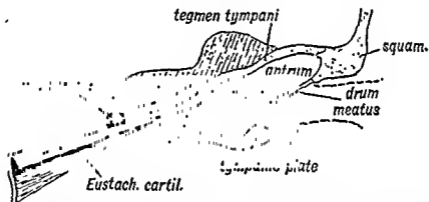


FIG. 280 Showing the Cavities derived from the Eustachian Recess of the Primitive Pharynx.

formed by the tympanic plate, is inflated into a bulla, the tympanic bulla. Its meaning is unknown, but when a bulla is developed the antrum of the mastoid is small or absent [7].

Auditory Ossicles.—In the 3rd month the auditory ossicles become clearly differentiated in cartilage within the mesodermal tissue between the meatal recess on their outer side and the Eustachian recess on their inner. Concerning their development, the exact researches of Broman [8], of Hammar, and of Jenkinson [9] give us a very full account. The malleus represents the upper or articular end of Meckel's cartilage (Figs. 282, 213); the incus, developed beyond the articular end of Meckel's cartilage, represents the cranial articular base—the quadrate of lower vertebrates. The stapes (Fig. 282) is developed at the upper end of the hyoid arch, the sides of the stirrup being formed round the dorsal end of the artery of the hyoid arch. Even in the 4th month of development the expanding cavity of the tympanum has only reached the handle

the 3rd arch, which, it will be remembered, also contributes to the formation of the soft palate. The Eustachian tube retains through life the ciliated epithelial lining of the primitive pharynx. Its inner two-thirds is bounded behind by a triangular plate of cartilage, which is attached at its inner or pharyngeal end to the internal pterygoid plate, by its outer to the tympanic ring, both of which are probably derived from the palato-quadrate bar (Fig. 208, p. 252). The cartilage is developed in the 4th month of foetal life. The tympanic plate grows inwards and forms the floor of the outer third of the tube (Fig. 280), while the periotic capsule (petro-mastoid) which is developed above and

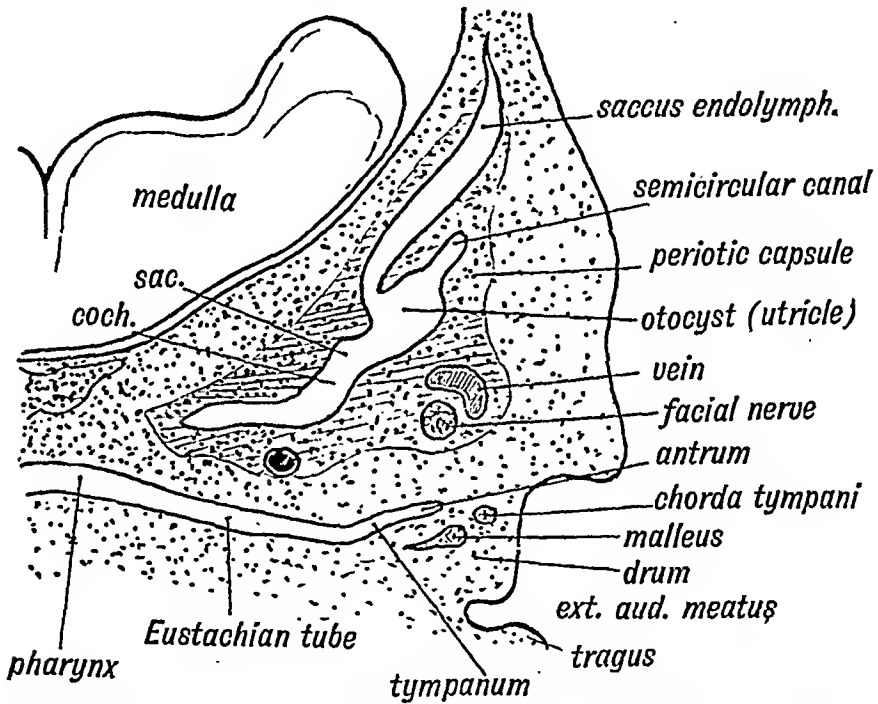


FIG. 279. Showing the condition of the Auditory Organs in a 7th-week Human Foetus. (After Siebenmann.)

behind the 1st cleft, grows forwards and forms the roof of its outer third. The part of the petro-mastoid which grows over it is the *tegmen tympani* (Fig. 274); it also forms the roof of the tympanum and of the antrum of the mastoid. The tensor tympani and tensor palati are developed on the mandibular side of the 1st cleft and are supplied from the nerve of the mandibular process through the otic ganglion.

The Tympanum.—The tympanum can scarcely be said to exist until the 3rd month of foetal life. Until then, the Eustachian recess ends in jelly-like tissue containing the cartilaginous bases of the malleus and incus. It is directed outwards and backwards between the periotic capsule to its posterior and inner side, and the external cleft depression (meatus) and developing squamosal to its outer (Fig. 279). As the

year the antrum may be buried by a plate of bone 20 mm. thick or more. There is a great individual variation, however, in the thickness of its outer wall. The antrum lies above and behind the level of the external auditory meatus; the post-auditory spine and supra-meatal triangle formed by the post-auditory part of the squamosal lie over it and serve as surface guides to it. The antrum opens in front into the attic of the tympanum. The tegmen tympani (Fig. 285) forms its roof and the petro-mastoid its floor and inner wall. The canal for the VIIth nerve runs down the inner wall of its mouth (Fig. 285), and in its inner wall is situated the external semicircular canal. The petro-squamosal suture in its roof (Fig. 284) and the masto-squamous suture on its outer wall (Fig. 216, p. 261) become closed in the second year, and thus the escape of pus from it is rendered more difficult. The rudiments of the mastoid cells are already present as evaginations or pits of the antral lining at birth (Arthur Cheatele).

Petro-Squamous Sinus.—We have seen (p. 200) that the primitive vein of the head, part of which persists as the cavernous sinus, escapes from the cranial cavity just in front of the auditory capsule. Before escaping from the skull it receives a tributary from the hind-brain—which afterwards occupies the petro-squamous suture. This vein, frequently of considerable size, runs forwards from the lateral sinus, and commonly ends in a tributary of the middle meningeal vein. It receives, as it runs along, venules from the antrum and attic and may be the means of carrying infection from the middle ear to the lateral sinus or to the meningeal veins (Cheatele). The petro-squamous sinus may open in man, as it does in mammals generally, at the post-glenoid foramen, situated at the outer end of the Glasserian fissure, near the base of the zygoma. The vein thus emerging may represent the primitive vein of the head.

Membrana Tympani.—As may be seen from Figs. 275, 279, the membrana tympani is of very considerable thickness until the gelatinous tissue in the tympanum is absorbed. It has an inner covering of endoderm and an outer of ectoderm. In the mesodermal tissue between the coverings lie parts of the malleus, incus and chorda tympani. As the gelatinous tissue round the fundus of the Eustachian recess is absorbed during the later months of foetal life, the membrane lining the tympanum becomes closely applied to and almost surrounds the handle of the malleus and chorda tympani. The membrana tympani is supported by the tympanic ring, the age changes of which have already been dealt with (p. 260). The membrane contains tissue derived from both mandibular and hyoid arches, and hence receives nerves and vessels from both. In tadpoles the cartilaginous ring in which the membrana tympani is set "induces" the ectoderm and other overlying tissues to

of the malleus (Fig. 281). The upper part of the drum (*pars flaccida*) is not yet differentiated. The attic, antrum, head of the hammer and body of the incus are still outside the cavity of the tympanum.

The **Antrum of the Mastoid** represents the extreme outer or posterior

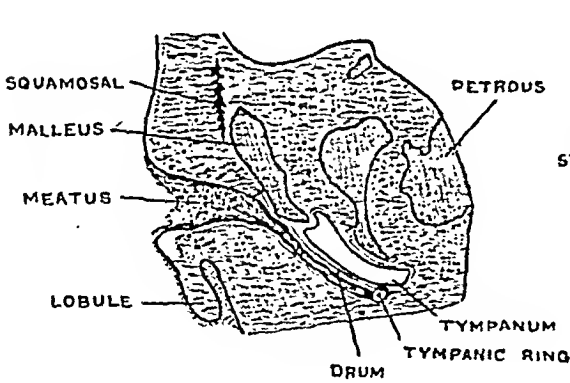


FIG. 281.

FIG. 281. Section of the External Auditory Meatus, Drum and Tympanum of a Human Foetus in the 4th month of development. The meatal plug fills the deep part of the meatus and only the handle of the hammer is in the tympanic cavity. (After Broman.)

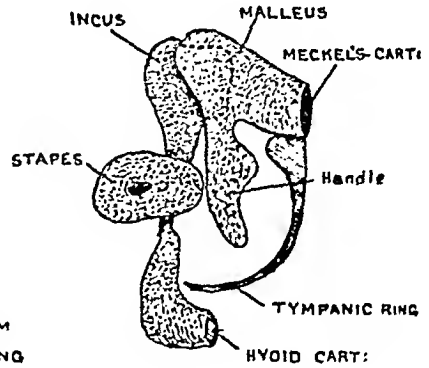


FIG. 282.

FIG. 282. The Auditory Ossicles of the Left Side, seen on their Inner Aspect, during the 3rd month of development. (After Broman.)

end of the chamber derived from the extension of the Eustachian recess (Figs. 279, 280, 281). It is formed during the 6th and 7th months by an expansion of the tympanic cavity upwards and backwards in the surrounding mucoid tissue. Its use is uncertain, but it has frequently to be

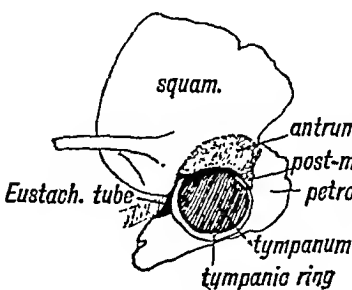


FIG. 283.

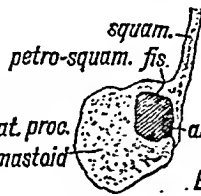


FIG. 284.

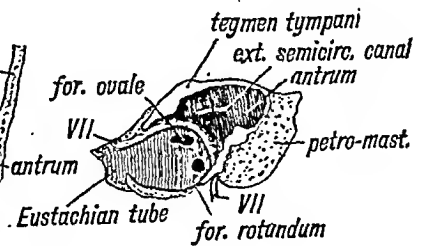


FIG. 285.

FIG. 283. The Temporal Bone at birth, showing the formation of the Antrum between the squamosal and petro-mastoid.

FIG. 284. A transverse section showing how the Walls of the Antrum are formed.

FIG. 285. Showing the outer aspect of the Petro-mastoid at birth after the squamosal is removed.

exposed by the surgeon to remove the effects of chronic middle-ear disease. At birth its outer wall is formed by the thin post-auditory part of the squamosal (Figs. 283 and 284). The squamosal forming its outer wall is then only 2 mm. thick, but every year until the 20th, or later, this plate increases nearly 1 mm. in thickness, so that by the 20th

currents in the semicircular canal as the head is moved, and so too do the movements of the stapes. The neuroblasts of the vestibular and cochlear ganglia, like those of a posterior root ganglion, send one set of processes to receive impulses arising in the hair cells and another set to transmit these impulses to nerve stations situated in the hind-brain. The hair cells thus become connected with the hind-brain by the auditory nerve fibres of the cochlear and vestibular ganglia. The otocyst clearly represents a sense organ which was primarily situated in the skin and through its hair-like processes was sensitive to stimuli which gave information regarding the position and movements of the body. Its auditory function arose at a later stage.

In the lower vertebrates, as in the earlier embryonic stages of the higher mammals, the otocyst is of a saccular form with a stalk above—the *ductus endolymphaticus* [10] (Fig. 287). The simplest form of

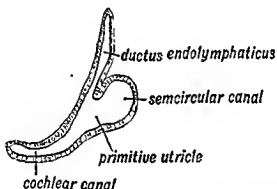


FIG. 287. The Otocyst in an Embryo of 5 weeks; it shows a demarcation into the primary parts of the membranous labyrinth

vertebrate otocyst is seen in the lamprey; the superior and posterior semicircular canals are present, but, as in the mammalian embryo, the primitive cyst is undivided into utricle, saccule and cochlear canal. The semicircular canals grow out from the vesicle as flat, hollow plates, but only the circumferences of the plates persist, the centres disappearing.

The development and differentiation of the human otocyst have been closely studied by Dr. G. Streeter [11]. In Fig. 288 three stages depicted by him are represented. In the 5th week there are three parts: (i) the ductus endolymphaticus, at one time regarded as the stalk which connected the cyst with the surface of the head, but now known to be an outgrowth formed after the stalk is obliterated; (ii) the vestibular pouch or part; (iii) the cochlear pouch or rudiment. By the 6th week a higher stage of differentiation is reached; all the parts of the adult labyrinth are indicated—the ductus and saccus endolymphaticus (both of uncertain import); the semicircular canals, with their ampullae; the

undergo differentiation during development, recalling the "evocation" of the lens by the optic cup.

Membranous Labyrinth.—The minute otic vesicle, which sinks under the ectoderm of the embryonic head, just above the dorsal end of the first visceral groove, early in the 4th week, has become divided by the beginning of the 3rd month into the complex of structures shown in Fig. 286. The labyrinth thus formed is made up of: (i) the utricle; (ii) three semicircular canals opening into the utricle; (iii) the saccule; (iv) a Y-shaped canal uniting the utricle and saccule—from the stem of which springs the ductus endolymphaticus (all of the foregoing parts constitute the vestibular or balancing part of the labyrinth); (v) the cochlear canal—the part connected with hearing. The labyrinth, as

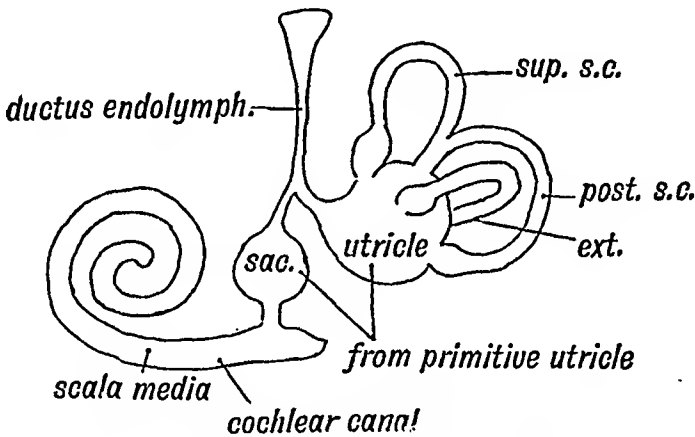


FIG. 286. Diagram of the Membranous Labyrinth.

we have just said, has a simple as well as a very early beginning. A certain area or placode of ectoderm, situated above and behind the first visceral groove and lying against what are regarded as the 4th and 5th neuromeres of the hind-brain (Figs. 101, 118) becomes invaginated during the 4th week. In this manner, and at this early date, there is formed a simple closed pyriform sac, the *otocyst*, which becomes surrounded by the tissues of the mesodermal capsule of the brain. The sac contains a fluid, the endolymph, and also otoliths are formed in it later. The otocyst lies at first close to the side of the hind-brain with the ganglionic mass belonging to the VIIth and VIIIth cranial nerves to its inner and anterior side (Fig. 118). The epithelial cells lining it, all of which are originally columnar, soon become flattened, except in certain areas, where they retain the columnar form and develop hair-like processes. The hair-like processes are to serve as levers and become capable of being moved by various means to evoke nerve stimuli. Under the influence of gravity otoliths serve to move them so do the

cochlear part—surrounding the cochlea. The course of the facial nerve indicates approximately their line of union. The cartilage of the cochlear part fuses with the parachordal or basilar cartilage; the vestibular part becomes continuous with the occipital plate (see p. 218). The otocyst has the power to “induce” the mesoderm that surrounds it to undergo chondrification [13].

Perilymph System.—The tissue which immediately surrounds the membranous labyrinth does not undergo chondrification, but becomes converted into an open meshwork of cells, the intercellular spaces containing perilymph. The chief or vestibular cistern of the perilymphatic system is formed round the saccule and utricle. In its tympanic or outer wall (Fig. 285) there is an oval area in which the *fenestra ovalis* and foot plate of the stapes are formed. Streeter [14] found that the vestibular cistern is the first to form, commencing at the stapedial plate when the foetus is 50 mm. in length (11 weeks old); an extension grows out along one side of the cochlear canal to form the *scala vestibuli*. Another area of the inner tympanic wall remains unchondrified, subsequently subdivided to form the *fenestra rotunda* (Fig. 285) and the *aqueductus cochleae*. In the 11th week a second cistern—the *scala tympani*—begins to form at the fenestra rotunda, growing along the side of the cochlear canal, opposite to the *scala vestibuli*, thus bringing that canal to lie between two perilymphatic spaces. The vestibular and tympanic extensions meet and fuse at the top of the cochlear canal, at the end of the 3rd month, thus forming the *helicotrema* [15].

Ossification of the Petro-mastoid.—About the end of the 4th month, when the labyrinth is not only differentiated but has attained its full dimensions, a series of ossific centres appear in the periotic capsule [16]; one of these, the *pteric*, gives rise to the bony tegmen tympani which forms the roof of the antrum, tympanum and Eustachian tube; the petro-squamous suture marks its outer edge; the hiatus Fallopii marks its junction with a second centre—the *opisthotic*. The centre forms the posterior or vestibular half of the petrous bone. The *pro-otic* forms the anterior or cochlear half; the mastoid part, which appears on the surface of the skull, is ossified from the *epiotic* centre. While the greater part of the petro-mastoid is formed in a cartilaginous basis, the dense layers which form the immediate bony capsule of the labyrinth, the modiolus and lamina spiralis of the cochlea, are laid down by the lining membrane of the perilymphatic space [17].

The Mastoid.—The mastoid part of the petro-mastoid is flat at birth; about the 2nd year the mastoid process appears as a slight knob, and it gradually grows downwards to form a cephalic lever for the sterno-mastoid, splenius and trachelo-mastoid muscles. The period of its

utricle and saccule. All of these are derived from the vestibular part of the otocyst. The cochlear rudiment has extended into a bent canal, and its communication with the saccule has become constricted to form the canalis reuniens. In the 10th week all parts are present, almost in their adult form. The utricle and saccule are now separated and only communicate by means of the ductus endolymphaticus [12]. The cochlear canal has assumed its spiral form.

The *primitive utricle* or vestibular pouch, which represents the main part of the otocyst, becomes subdivided into the saccule and utricle (Fig. 288, C, C', C''). The division occurs at the entrance of the endolymphatic canal, which thus comes to open into both saccule and utricle.

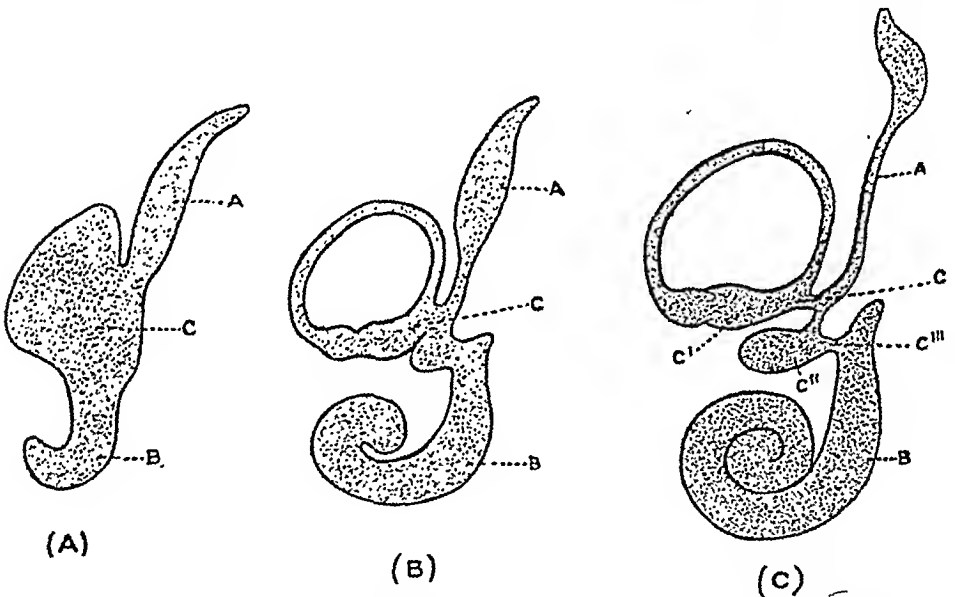


FIG. 288. Three stages in the development of the Human Membranous Labyrinth. A, at the end of the 5th week; B, at the end of the 6th week; C, at the end of the 10th week. (Streeter.)

The endolymphatic duct is enclosed in the petro-mastoid, its extremity appearing at the hiatus vestibuli, where it ends beneath the dura mater in a dilatation. The cochlear canal (scala media), the real auditory part of the labyrinth, although late in point of evolution, is not late in its developmental appearance. There is merely a rudiment of the cochlea in fishes and in amphibians. In reptiles, birds and monotremes it is a straight canal—the *Lagena*. Only in mammals is it arranged spirally. In it the organ of Corti is developed.

Periotic Capsule.—The mesoderm surrounding the membranous labyrinth and dorsal aorta (internal carotid) becomes cartilaginous at the end of the 2nd month of foetal life, forming the periotic capsule (Fig. 279). There are two centres of chondrification, one for the vestibular part—surrounding the vestibular division of the labyrinth, and one for the

Organ of Corti.—In Fig. 289 is given a diagrammatic section across the cochlear canal to show the manner in which its ectodermal lining is modified to form the organ of Corti—the machinery concerned in producing auditory stimuli. The canal has become three-sided—one side lying against the scala vestibuli (vestibular wall), another against the scala tympani (tympanic wall), the third being peripheral or outer. The ectoderm on the vestibular wall atrophies and disappears—the fibrous base forming Reissner's membrane. The ectoderm on the outer wall is modified to form a secretory apparatus—the vascular body (*striae vasculares*) [18]. On the tympanic wall the ectoderm is modified to form: (a) hair or sensory cells; (b) supporting or pillar cells—comparable to neuroglial cells in the spinal cord, and fibres of Müller in the retina; (c) tectorial cells, producing a peculiar cuticular substance, which forms the tectorial membrane—in which the hair process of the sensory cells are embedded. The auditory nerve fibres commence round the hair cells [19].

In the sacculæ, utricle and ampullæ of the semicircular canals, the hair cells are planted on a fixed base, their hair-like processes being moved by otoliths acting under the influence of gravity, or by currents set up in the semicircular canal. The hair cells of the cochlea, on the other hand, are planted on a movable base—the basilar membrane, which responds to every movement of the stapes, because of the displacement of perilymph in the adjoining scalæ. The tectorial membrane bends the hair-like processes with every movement of the basilar membrane, because the tectorial membrane is attached to a fixed base on the spiral bony lamina while the hair cells rest upon a movable one.

Ganglia of the Labyrinth.—The origin of the mass of nerve cells lying between the otocyst and hind-brain has already been mentioned (p. 323). They arise from the neural crests and from adjoining placodes. The ganglionic mass becomes divided into three parts: (i) the *geniculate ganglion* of the facial nerve, which is included in the petro-mastoid, but has no functional relationship to the labyrinth; it gives rise to the great superficial petrosal nerve, chorda tympani and pars intermedia (root part of ganglion) in the same manner as a ganglion of the posterior root produces the sensory fibres of a spinal nerve (Dixon) (Fig. 118); (ii) the *vestibular part*—applied to the vestibular portion of the labyrinth; (iii) the *cochlear part*, which becomes applied to the cochlear canal (scala media). The differentiation of the vestibular and cochlear ganglionic masses proceeds at the same rate as the development of the membranous labyrinth [20].

In Fig. 290 four stages in the differentiation of the nerve equipment of the ear are reproduced. The figures are those of Dr. George

most active growth is marked by the eruption of the permanent teeth. In anthropoids the mastoid grows out as a flat, wing-shaped process continuous with the occipital crest, and thus increases the basal area of the skull on which the neck muscles are inserted (Fig. 179). The post-auditory process of the squamosal forms a considerable part of the mastoid process; it reaches to the apex and forms the anterior border (Fig. 216, C). As the mastoid process grows the diploic spaces within it enlarge into air spaces. Those round the antrum come to open into it, but the more distal remain closed. These spaces occupy the whole of the mastoid part of the temporal, but they also extend forwards in the post-auditory process of the squamosal, and may spread backwards to the occipital. Three varieties of mastoids are recognized: (i) dense

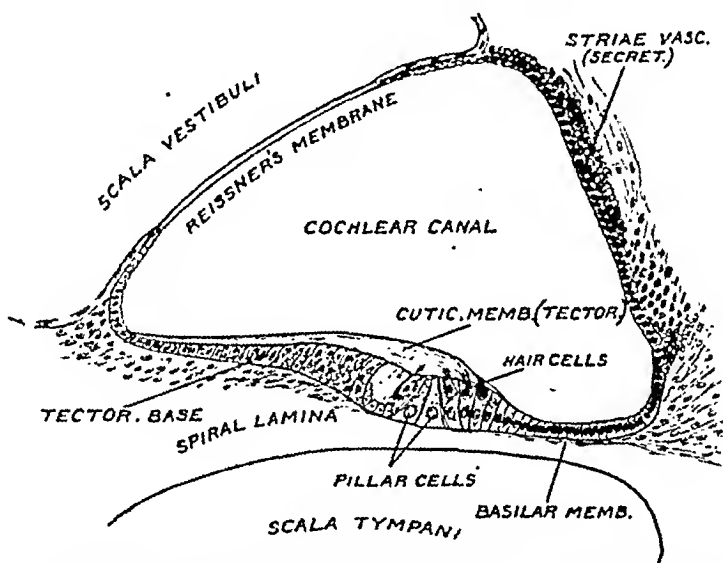


FIG. 239. Diagrammatic section across the Cochlear Canal of a newly born Child to show the differentiation of ectodermal epithelium to form the Organ of Corti. (After Keibel.)

processes in which the air cells are minute or absent (infantile type of Cheatele); (ii) a type containing numerous large spaces (pneumatic); (iii) an intermediate type with large cells round the antrum and a few small ones near the surface. The third type is the commonest.

Floccular or Subarcuate Fossa.—At birth there is a fossa situated on the posterior aspect of the petro-mastoid. It is filled with a process of the dura mater in the human embryo, but in all except the highest primates it contains the paraflocculus (Fig. 113), a part of the cerebellum which is quite vestigial in man. The posterior semicircular canal surrounds the fossa. This is the condition in most mammals throughout life, but soon after birth the fossa becomes closed in man, merely a remnant being seen above and internal to the hiatus vestibuli in the bone of the adult.

vestibular and cochlear ganglia correspond to those of posterior spinal roots. The nuclei or centres in which the vestibular and cochlear roots end correspond to those in which fibres of the spinal roots end—the gracile and cuneate nuclei of the spinal cord. The relays from the vestibular nuclei differ from those of the cochlear nuclei in the following way. The relays from the vestibular nuclei proceed to the cerebellum, to centres that preside over the movements of the eyes (by the longitudinal bundle) and to the motor centres of the spinal cord (vestibulo-spinal tracts). The relays from the cochlear nuclei, like those from the gracile and cuneate nuclei, proceed to the thalamus, to that part of it known as the median geniculate bodies [22]; and also to the inferior

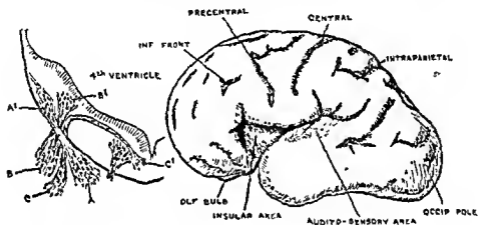


FIG 291.

FIG 292

FIG. 291. Section of the hind-brain showing the end of the cochlear nucleus and the Vllth nerve.

FIG. 292. Lateral view of the Cerebrum of Fœtus in the 7th month of development. (Retzius) The audito-sensory area on Heschl's gyri is stippled.

colliculi of the mid-brain. In this the cochlear relays resemble the termination of the optic tracts in the lateral geniculates and superior colliculi. The bipolar cells of the retina correspond to the cells of the cochlear nuclei.

Nerve Centres. (i) *Cochlear or auditory.*—By the end of the 5th week (Fig. 291) the ingrowing root fibres of the cochlear ganglion have reached a central mass of nerve cells (central cochlear mass) developed in the alar lamina of the hind-brain. The central cochlear ganglion gives rise to the acoustic tubercle (situated on the restiform body) and a lateral accessory nucleus on the outer aspect of the restiform body. By means of the lateral fillet the cochlear central stations are united with the superior olive, inferior colliculus (mid-brain) and internal or medial

Streeter [21] and represent stages in the 1st, 2nd and 3rd months of development. Towards the end of the 1st month the cochlear part becomes apparent (*A*); in the 2nd month this part is undergoing rapid growth (*B*); early in the 3rd month (*C*) it has assumed a spiral form, and lies within the spiral lamina of the cochlea, and hence is often named the spiral ganglion. The cells of the spiral ganglion send out two sets of processes—to the organ of Corti (peripheral fibres), to cochlear nuclei situated in the hind-brain (root fibres). The cochlear fibres form the lateral root of the VIIIth nerve. The vestibular ganglionic mass becomes subdivided into a dorsal mass—connected with the areas of sensory cells

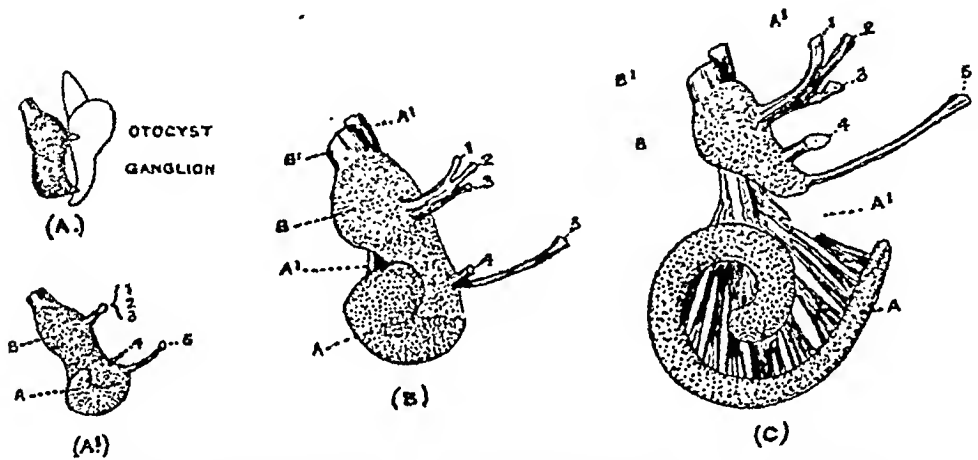


FIG. 290. The Differentiation of the Ganglion of the Labyrinth. (Streeter.)

A. The otocyst and ganglion of a human embryo in the 4th week. *A'*. In the 5th week. The parts are those of the left side, and are viewed on their lateral aspect. *B.* From a foetus in the 7th week (16 mm. long). *C.* From a foetus in the 9th week (30 mm. long).

1. Nerve to ampulla of superior canal.
2. Nerve to ampulla of lateral canal.
3. Nerve to utricle.
4. Nerve to saccule.
5. Nerve to ampulla of posterior canal.

A. Cochlear ganglion.
B. Vestibular ganglion.

A'. Cochlear nerve.
B'. Vestibular nerve.

in the utricle and the ampullae of the superior and external semicircular canals (Fig. 290, 1, 2, 3), and a lower or ventral mass, which sends fibres to the saccule and posterior semicircular canal. The vestibular ganglion is lodged in the fundus of the internal auditory meatus. Its ingrowing or centripetal fibres form the mesial root of the VIIIth nerve. While the cochlear root enters the floor of the 4th ventricle superficial to the inferior peduncle of the cerebellum, the vestibular or mesial root passes deep to it. The lateral or cochlear root is connected with hearing, the mesial or vestibular with balancing.

As an introduction to the paragraphs that are to follow, it may be well to remind readers that in the ear there are structures serving two different offices, one very old (the vestibular) and one recent from an evolutionary point of view (the auditory). We have seen that the

the ear in the living embryo without being struck by their developmental behaviour. Otocyst and ganglia seem to seek out each other and come together; nerve centres and nerve communications become established in the hind-, mid- and fore-brains; finally a connection is established between the thalamus and pallium or cortex. We must note, too, that parts of the fish-like pharynx and of the piscine apparatus of mastication have been taken over by the organ of bearing. Of the evolutionary and developmental means of bringing about these structural and adaptational changes we have still much to learn.

Summary.—A study of the development and evolution of the human ear leads to the following conclusions:

- (i) That the otocyst was originally an external sense organ connected with the balancing of the body; it became encysted above the 1st visceral cleft, and part of it became sensitive to sound waves.
- (ii) Parts of the dorsal laminae of the hind-brain were connected with it, and from those were developed the acoustic ganglia and nuclei, and probably also the cerebellum (see pp. 133, 150).
- (iii) The 1st and part of the 2nd clefts were modified in air-breathing forms, to become air passages for transmitting sounds.
- (iv) Parts of the skeletal bases of the 1st and 2nd visceral arches became the auditory ossicles.
- (v) The external ear represents a new structure which arose round the upper part of the 1st visceral cleft. It came with the evolution of mammals.

NOTES AND REFERENCES

[1] For the development and evolution of the ear, see Streeter, G. L., *Jour. Exp. Zool.*, 1906, 3, 543; 1907, 4, 431; 1914, 16, 149; *Amer. Jour. Anat.*, 1907, 6, 139; 1907, 7, 337; Keith, Sir A., *Wrightson's New Theory of Hearing*, 1920; Frazer, J. E., *Manual of Embryology*, 1940; Evans, H. M., *Proc. Roy. Soc.*, 1932, 111 (B), 247 (hearing in fishes).

[2] Frazer, J. S., *Archiv. Otolaryng.*, 1931, 13, 1.

[3] For the development of the external ear, see Streeter, G. L., *Contrib. Emb.*, 1932, 14, 113. Prof. Wood-Jones, in reporting with Mr. Wen i'Chuan on the occurrence of congenital fistulae in the ears of Chinese (*Jour. Anat.*, 1934, 68, 525), expressed the opinion that the tragus was the only part of the external ear which is of mandibular origin, the remainder arising from tissues of the hyoid arch. The tragus alone is supplied by the nerve of the mandibular arch. Fistulae occur usually either above or below the tragus, in the line of the hyo-mandibular cleft. The distribution of the branches of the facial nerve support Wood-Jones's view (see Fujita, T., *Anat. Anz.*, 1934, 78, 321). So, too, do observations by J. P. Scott on the ear of the guinea-pig (*Amer. Jour. Anat.*, 1936, 60, 397).

[4] For literature on fistulae of the auricle, see Maria de Olivera, *Trab. Soc. Portug. Antrop. Etnol.*, 1921, 1, 85; Frazer, J. S., see under note [2]; Congdon and Others, *Amer. Jour. Anat.*, 1932, 51, 439 (170 cases); Wood-Jones, F., see preceding note.

geniculate body (thalamencephalon) of the opposite side. Projection fibres connect the geniculate body with the cortex of the 1st temporal gyrus (see Fig. 142). Heschl's gyri (audito-sensory) of the 1st temporal convolution are already apparent at the beginning of the 7th month (see Fig. 292). The cortex of these gyri, with the neighbouring area of the 1st temporal, receives the fibres from the internal geniculate nucleus, and forms the audito-sensory areas [23]. It is highly probable that the cortex of the greater part of the temporal lobe forms association areas, for the interpretation of sounds. The auditory centres are necessarily connected with the centres for sight, movement and speech, but the development of these connections is as yet imperfectly known.

(ii) The ingrowing fibres of the vestibular ganglion pass beneath the inferior peduncle of the cerebellum to terminate in the nerve cells of the deeper nuclei in the floor of the 4th ventricle known by the names of Bechterew and of Deiter (Fig. 291). These nerve cells and fibres are in no sense auditory, but concerned with the balancing of the body. The vestibular nuclei on the floor of the 4th ventricle are connected, by the posterior longitudinal bundle and other tracts, with motor nerve centres situated in the central system, from the oculo-motor nucleus above to the sacral centres below. Through the inferior peduncle of the cerebellum, the nuclei in which the vestibular root ends are also connected with both the vermis and lateral cerebellar lobes. The cerebellum and acoustic ganglia arise from the same part of the hind-brain; there is a close developmental relationship between the origin of the vestibular or balancing part of the ear and the cerebellum.

Internal Auditory Meatus.—The internal auditory meatus is formed round the VIIIth nerve, its ganglia, and the VIIth nerve. The falciform crest separates the fibres of the dorsal and ventral parts of the vestibular nerve. The meatus also contains a prolongation of the arachnoid and subarachnoid space. Fractures of the base of the skull frequently cross the petro-mastoid in the line of the internal auditory meatus, vestibule and membrana tympani. In such cases the cerebro-spinal fluid and perilymph may escape by the external auditory meatus.

Machinery of Development.—The otocyst has within it the power of differentiation; when excised from a chick embryo of three days and grown in artificial media, the otocyst passes through the normal stages of development [24]. Dr. George Streeter [25] observed that the otocyst of the tadpole possessed the power to change its position, and carried out experiments to test its ability to recover a normal position after disturbance. The otocyst has such powers, and seems also to be able to compel the mesoderm in which it may be placed to form a cartilaginous capsule [26]. One cannot observe the assemblage of the parts that form

CHAPTER XVIII

PHARYNX AND NECK

In previous chapters the origin of various pharyngeal structures has been touched on. We have seen that a forward prolongation of the archenteron during the 3rd week gives rise to the fore-gut (Fig. 21), that the anterior or pharyngeal part of the fore-gut is separated from the primitive mouth or stomodaeum by the oral plate (Fig. 129), that the notochord is laid down along the dorsal wall of the pharynx (Fig. 129) and that the heart lies under its floor, while the aortic arches encircle it (Fig. 101). Mention has been made of its cartilaginous skeleton (Fig. 181), of the segmentation of its mesoderm (Fig. 180) and of its nerves (Fig. 118). In this chapter we have to knit these isolated statements together by following the developmental changes that transform the simple fish-like pharynx of the embryo into the complex of structures found in the neck and throat of the adult.

Evolution of the Pharyngeal Region.—In the latter part of the 1st month and opening part of the 2nd, the neck of the human embryo undergoes a very remarkable transformation. In the 5th week, when the human embryo is about 5 mm. in length, representations of gill or branchial clefts and gill or branchial arches are plainly to be seen in the region of the neck or pharynx (Fig. 293); the elevation caused by the heart reaches forward almost to the mandibular arch; properly speaking, there is no neck at the 4th week. ^{directly} 78). all
lead of
region,
begun
the fore-gut to form the larynx, trachea, bronchi and lungs (Fig. 295). On passing from the 6th to the 7th week of development, we see the human embryo evolve from a stage in which the parts are adapted for a branchial respiration, as in fishes, to a higher one in which its parts are fitted for breathing air. Pharyngeal glands, such as the tonsil, thyroid and thymus, originally developed in connection with the visceral or gill arches, become modified in structure and position to suit the new conditions of life. With the evolution of the mammalian method of mastication and swallowing, the pharynx, originally a respiratory

[5] Quelprud, T., *Zeitsch. Morph. Anthropol.*, 1934, 34, 360 (inheritance of Darwin's tubercle).

[6] Prof. Frazer's observations on the development of the Eustachian tube find support in those made on Sphenodon by the Rev. F. J. Wyeth (*Phil. Trans.*, 1924, 212 (B), 259).

[7] van der Klaaw, *Bull. Amer. Mus. Nat. Hist.*, 1931, 62, 1-352.

[8] For development of auditory ossicles, see Frey, Hugo, *Anat. Hefte*, 1911, 44, 363; Broman, I., *Normale und Abnormale Entwicklung des Menschen*, 1911; *Entwicklung des Menschen*, 1927.

[9] Jenkinson, J. W., *Jour. Anat.*, 1911, 45, 305; Marcus and Others, *Zeitsch. Anat. Entwickl.*, 1933, 100, 149; Anson and Others, *Anat. Rec.*, 1934, 61 (suppl. 2) (stapes); Schimert, J., *Anat. Anz.*, 1933, 76, 317 (development of the stapedius muscle).

[10] See Anson and Wilson, *Anat. Rec.*, 1936, 65, 485; Anson and Black, *ibid.*, 1934, 58, 127; Anson, B. J., *ibid.*, 1933, 57, 53.

[11] Streeter, G. L., see references under note [1]; see also Anson, B. J., *Anat. Rec.*, 1934, 59, 15; Burlet, H. M., *Zeitsch. Anat. Entwickl.*, 1935, 104, 79 (evolution of horizontal canal).

[12] Dr. T. H. Bast has described a valve-like structure at the opening of the utricle into the ductus endolymphaticus (*Anat. Rec.*, 1928, 40, 61; 1937, 68, 75).

[13] For an account of the various "inductive" phenomena seen in connection with the development of the ear, see references to Needham, Huxley and De Beer, and other authorities given in note [1], Chapter IV; also Kaan, Helen W., *Jour. Exper. Zool.*, 1938, 78, 159; Schmidt, C. A., *Archiv. de Biol.*, 1936, 48, 361.

[14] *Contrib. Emb.*, 1918, 7, 5.

[15] Streeter, G. L., *Amer. Jour. Anat.*, 1917, 21, 299; *Contrib. Emb.*, 1918, 7, 5; Foley, L. D., *Anat. Rec.*, 1931, 49, 1.

[16] Bast, T. H., *Contrib. Emb.*, 1930, 21, 53; *Archiv. Otolaryng.*, 1936, 23, 509.

[17] For an account of the peculiar form of ossification in the petrous bone, see reference to T. H. Bast in preceding note.

[18] Fieandt and Saxém, *Zeitsch. Anat. Entwickl.*, 1937, 106, 424.

[19] van der Stricht, O., *Contrib. Emb.*, 1920, 9, 109; Keith, Sir A., see reference in note [1].

[20] Cameron and Milligan, *Jour. Anat.*, 1910, 44, 111.

[21] Streeter, G. L., *Amer. Jour. Anat.*, 1907, 6, 139; Bartlemez, G. W., *Jour. Comp. Neur.*, 1922, 34, 201; van Campenhout, E., *Archiv. de Biol.*, 1935, 46, 273 (origin of vestibular and cochlear ganglia); Weston, Jean K., *Jour. Anat.*, 1939, 72, 263; Hardy, Mary, *Anat. Rec.*, 1934, 59, 403; Wolff, Dorothy, *Amer. Jour. Anat.*, 1936, 60, 55.

[22] Clark, W. E. Le Gros, *Jour. Anat.*, 1933, 67, 536; see also Papez, J. W., *Jour. Comp. Neur.*, 1936, 64, 41; Walker, A. E., *Jour. Anat.*, 1937, 71, 319.

[23] For connections of vestibular and cochlear ganglia, see Woollard's *Recent Advances in Anatomy*, 1927, Chapter X.

[24] Fell, Honoria B., *Archiv. Exper. Zellforsch.*, 1928, 7, 69; see also references given in note [13].

[25] Streeter, G. L., *Jour. Exper. Zool.*, 1914, 16, 149; *Anat. Rec.*, 1921, 21, 115.

[26] For earlier papers, see Ogawa, C., *Jour. Exper. Zool.*, 1921, 34, 17; Greene and Laurens, *Amer. Jour. Physiol.*, 1923, 64, 120; Regan, F. P., *Jour. Exper. Zool.*, 1917, 23, 85.

pharynx is bounded by *visceral* or *pharyngeal arches* [1], which are separated by depressions or grooves (human embryos) or clefts (fishes); in both the heart is situated under the pharynx, and from the ventral aorta, aortic arches pass up on each side, one in each visceral arch, to terminate in the dorsal aortae. It is true that all the aortic arches are not present in the human embryo at one time: the anterior disappear as the posterior form. In fishes the aortic arches give off vessels to the gills, in which the blood is arterialized. In the human embryo the blood passes directly through the aortic arches. The walls of the pharynx were, therefore, primarily respiratory in function.

A considerable part of the human neck is formed from the embryonic visceral arches. A knowledge of the transformation of the embryonic to the adult pharynx is of practical importance: it helps us to understand why fistulae and cysts are sometimes found in the neck; it accounts for the peculiar course taken by nerves such as the recurrent laryngeal and phrenic; it explains the peculiar distribution of nerves to the pharynx; and throws light on the nature and anomalies of the thymus, thyroid and tonsil. As may be seen from Fig. 293, the floor of the pharynx of the human embryo rests on the dorsal wall of the pericardium; in the adult the pharynx and pericardium are separated by the whole length of the neck. This separation begins at the end of the 6th week.

Visceral Arches.—The visceral arches bound and form the whole thickness of the wall of the primitive pharynx, which is flattened dorso-ventrally, so that its cavity forms a transverse cleft when seen in cross-sections of the embryo. Four arches, each bounded behind by a depression, are to be recognized superficially on each side of the pharynx of the 5th-week human embryo (Fig. 293), but behind the 4th groove are 5th and 6th arches, which, however, never become raised or superficially differentiated from the body-wall behind (Fig. 296). Sagittal and coronal sections of the primitive pharynx (Figs. 295 and 296) give a better idea of the arrangement and constitution of the visceral arches than can be had from a surface view. They are developed round the most anterior part of the fore-gut, which forms the lining membrane of the primitive pharynx. The pharyngeal lining membrane, therefore, is the same as that of the alimentary canal from which spring all the organs and glands of digestion and assimilation.

Visceral Grooves and Recesses.—The epithelium or endoderm, which lines the primitive pharynx, covers the inner aspects of the arches and passes outwards in the recesses between them, and there, for a short time, comes in contact with the epithelial covering of the body (ectoderm), which dips in to meet it (Fig. 296). The membrane thus formed by the union of the ectoderm and endoderm in the recesses between the arches

structure, was further modified. The tongue became differentiated from parts in the floor of the pharynx, and muscles which were at first

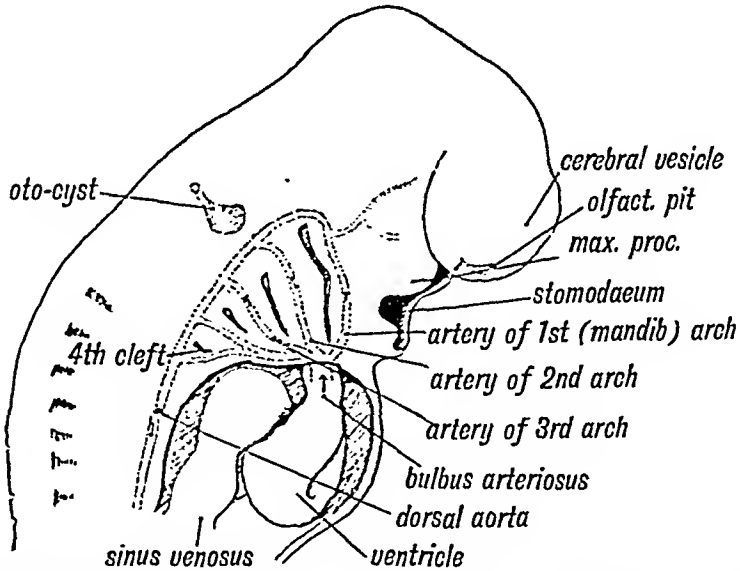


FIG. 293. Showing the Arches and Grooves on the Pharyngeal Wall of a Human Embryo at the beginning of the 5th week. Each arch contains an aortic arch. (After His.)

designed to move the branchial arches became converted into muscles of deglutition.

Pharynx of the Embryo.—There is very little resemblance between the

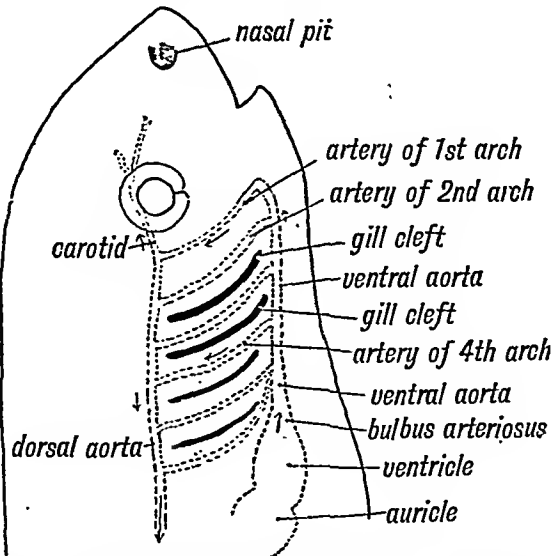


FIG. 294. Showing the position of the Heart, Visceral and Aortic Arches in a Fish. (Diagrammatic—after Gegenbaur.)

pharynx and neck of a human embryo in the 4th week and that of the adult. Indeed at this time the human pharynx resembles closely that of a fish (Figs. 293, 294). In both the human embryo and fish the

"cleft depression," on its inner side a "pharyngeal recess," presently developed into a pouch. From the endodermal lining of the pharyngeal pouches we shall see that the tonsil, thyroid and thymus arise: from the external depressions are formed the various branchial cysts and fistulae which occasionally occur in the neck of the adult. Further, at the upper end of each cleft depression there develop remarkable sense-organs, known as the *epibranchial placodes* (Fig. 298, A). In each arch there develop exactly the same elements as are to be seen in the gill arches of fishes, namely:

(a) A skeletal basis of *cartilage*; (b) an *aortic* or *vascular arch*; (c) a *larger nerve* along its anterior border and a *smaller* along its posterior; (d) a *muscle element* [2].

In Fig. 180 (p. 230) a schematic transverse section of the head region of a vertebrate embryo has already been given to show the relationship of a visceral segment or branchiomere to the cavity of the fore-gut.

The 1st visceral arch is known as the *mandibular*, the 2nd as the *hyoid* (Fig. 296). The remaining four are *branchial* arches, having been at one stage of evolution devoted solely to the purpose of carrying gills. The hyoid arch is specialized in fishes so as to provide a cover or operculum for the branchial arches, and assist in the circulation of blood through the gills and water through the pharynx. The mandibular arch bounds the rim of the buccal cavity in all vertebrates, and forms part of the apparatus of mastication.

Formation of the Cervical Sinus.—The 1st arch especially, and also the 2nd, grow—

The 2nd grows, at the c

sinking in of the hinder arches, and it is easy to see that as the hyoid arch grows backwards over them, an ectodermal space will become enclosed, this enclosure being known as the cervical sinus—representing the gill cavity of fishes. Its formation is effected in the 6th and 7th weeks. In Fig. 297 a model of the lining membrane of an embryo at the end of the 6th week of development is depicted as seen on its ventral aspect.

The enclosed space is to be a *vesicle*. The last-named connection is short-lived; indeed, before the end of the 2nd month all traces of the sinus itself should have disappeared.

Are the 3rd and 4th arches completely buried in the neck? Very careful studies made by Prof. J. E. Frazer [3] have convinced him that the subsidence of the 3rd arch is only partial. The condition he found

may be named the "cleft membrane." It is never ruptured nor disappears in the development of mammals, but is invaded by the meso-

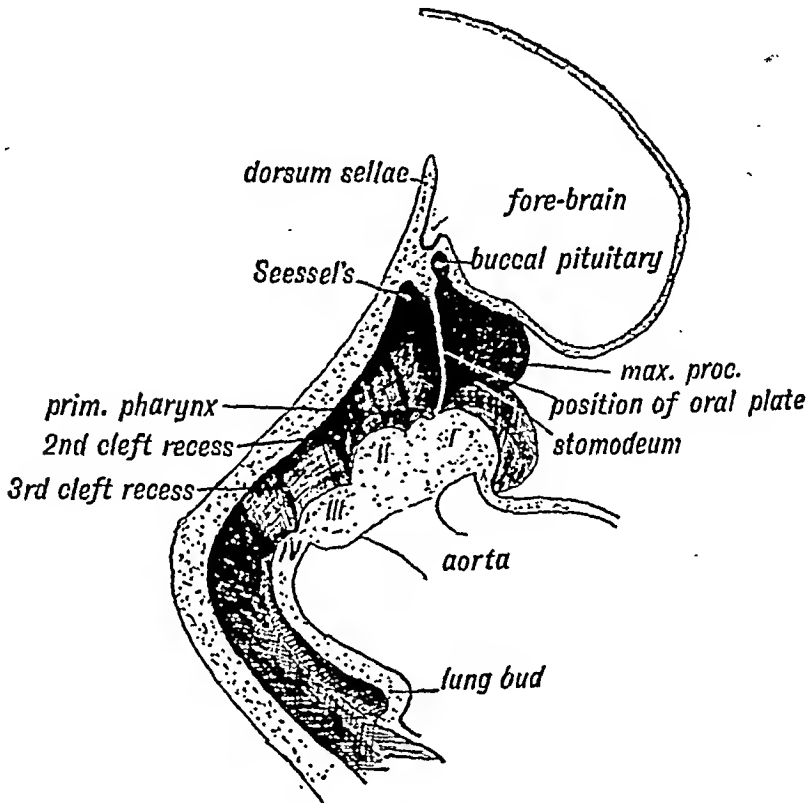


FIG. 295. Showing the Primitive Pharynx of a 5th-week Embryo in sagittal section, bounded by the Visceral Arches. (After His.)

derm of neighbouring arches ; in fishes it disappears and real clefts are formed between the arches. On the outer side of the membrane is the

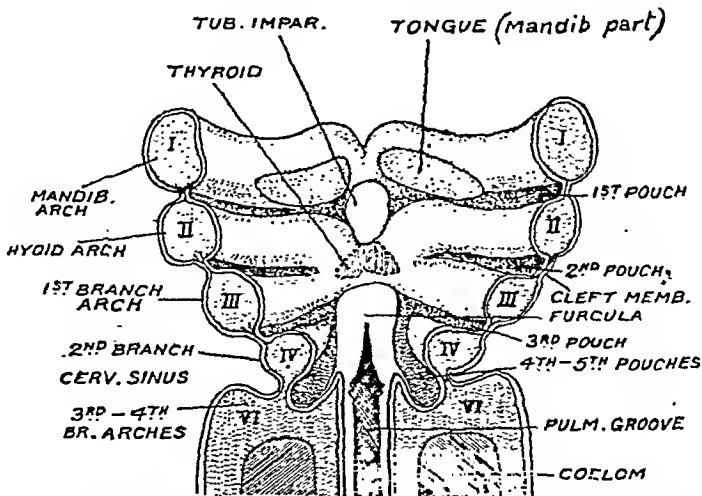


FIG. 296. Showing the Floor of the Pharynx of a 5th-week Human Embryo. (After His.) The sections of the visceral arches are marked by Roman numerals.

contact with the tonsillar recess, passing between the internal and external carotid arteries or in contact with the pharynx behind the hyoid (Fig. 299), connections that are explained by the relationship shown in Fig. 298. Often the cutaneous orifice is marked by a tag of skin representing a rudimentary external ear, which encloses a piece of cartilage [4]. If the outer cleft depression in front of or behind the 3rd arch persists, it must open in the cervical sinus or pit representing part of that sinus.

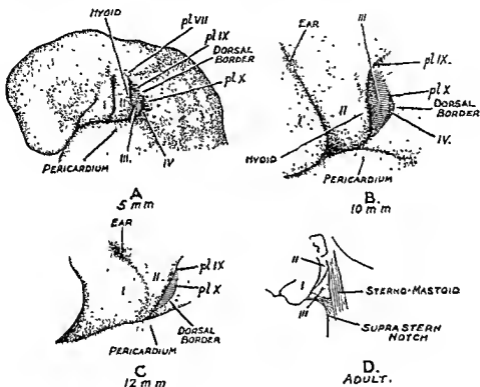


FIG. 298.

A. Neck of a Human Embryo at the end of the 4th week.

B. 10 mm

C. 12 mm

D. ADULT.

C. The End of Subsidence in the 7th week, leaving part of the 3rd arch exposed. The placodal areas are buried; so is the 4th arch (Prof. Frazer.)

D. The Areas of the Adult Neck formed from the 2nd and 3rd arches (Prof. Frazer.)

What becomes of the Visceral Recesses.—By the end of the 2nd month all pockets and recesses have disappeared from the interior of the pharynx of the human embryo, except the upper part of the 1st. From the external depression of the 1st cleft a solid ingrowth of epithelium takes place, which, ultimately becoming canaliculized, forms the *external auditory meatus* (Fig. 275). In connection with the upper or dorsal parts of the 1st and 2nd cleft depressions the *Eustachian tube* and

at the end of the 5th week is shown in Fig. 298, *A*. The 3rd and 4th arches form the floor of a small depressed triangular field. The anterior border is formed by the hyoid arch; the hinder or dorsal border is formed by an occipital fold; the lower by a pericardial border. The placodal areas of thickened epithelium at the cranial ends of the 2nd, 3rd and 4th arches are indicated. In Fig. 298, *B*, the state of the triangular cervical field is shown a week later. All three borders—hyoid, occipital and pericardial—have encroached on the field; the 4th arch is buried, but a recess leads to its placodal area. The condition reached a week later still is shown in Fig. 298, *C*; the occipital and pericardial folds

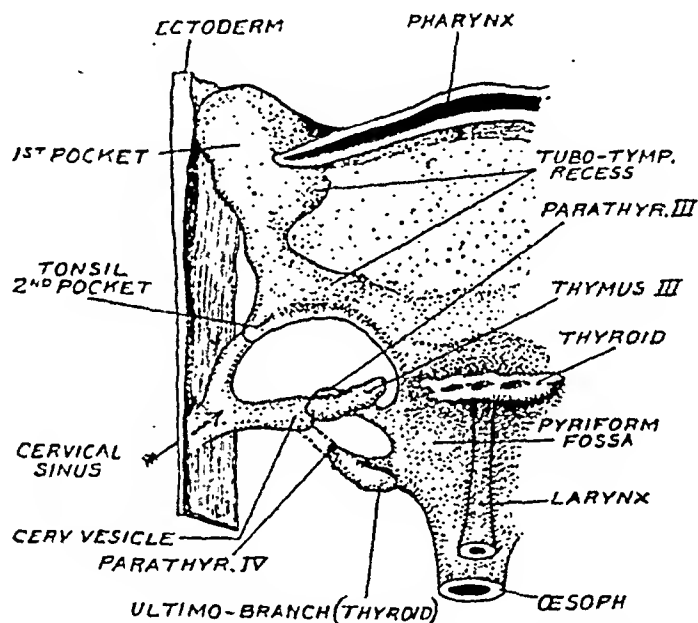


FIG. 297. The Lining Membrane of the Pharynx of a Human Embryo at the end of the 6th week of development (10 mm.) viewed on its ventral aspect. (Grosser.)

have disappeared, but the anterior or hyoid border is still in evidence; behind this border lies still exposed on the surface of the neck an area of the 3rd arch. This area, Prof. Frazer believes, will enlarge until it extends over the anterior triangle of the neck (Fig. 298, *D*). The sterno-mastoid muscle is developed just behind the triangular cervical field; if there is a persistence of placodal or of any developmental pocket, it should appear along the anterior border of the sterno-mastoid.

Although the various ectodermal structures that become enclosed during development of the neck usually disappear, yet they may persist and give rise to cysts or fistulae. They usually open along the anterior border of the sterno-mastoid, the commonest site being a short distance above the sterno-clavicular joint. The representative of the cervical sinus may be drawn out into a trumpet-shaped tube, which ends in

the laryngeal aperture, marks the sites of the 3rd and perhaps also the 4th inner cleft recesses (Fig. 312).

Cartilages of the Arches (Fig. 301).—The history of the skeletal basis of the 1st arch (Meckel's cartilage) has already been traced (p. 256).

The cartilage of the 2nd or *hyoid arch* forms (Fig. 301) :

(i) The *tympano-hyal*, embedded in the petro-mastoid, and originally continuous with the ear ossicles (Fig. 282). (ii) The *stylo-hyal*, which ossifies in the early years of life and becomes joined to the tympano-hyal

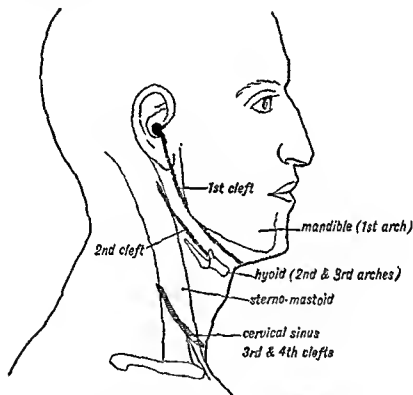


FIG. 300 Showing the position of the External Cleft Depressions in the Adult
(For explanation, see text.)

to form the styloid process. (iii) The segment below, the *epi-hyal*, becomes ligamentous, and forms the stylo-hyoid ligament, but it also may become ossified. (iv) The lowest segment, the *cerato-hyal*, forming the small horn of the hyoid [5]. The *epi-hyal* lies behind and outside the tonsil, and when ossified has been excised under the belief that it was a foreign body. The body of the hyoid (*basi-hyal*) represents the fused ventral parts (copulae) of the 2nd and 3rd cartilages; in the floor of the embryonic pharynx (Fig. 296) the ventral ends of the 2nd and 3rd arches end in a common or mesobranchial field. In this area the body of the hyoid develops just behind the tract of the thyro-glossal duct.

*tympa*num are formed, the *membrana tympani* remaining approximately in the position of a cleft membrane (p. 325).

If traces of the other clefts remain as fistulae or cysts we should expect them to appear in the positions shown in Fig. 300, that is, if the 3rd arch becomes buried and a cervical sinus formed, as we have hitherto believed [3]. Part of the 2nd cleft is marked in the goat by an opening and auricular appendage. In human beings the dorsal part of the 2nd cleft may persist, an auricle becoming developed on it, while the normal

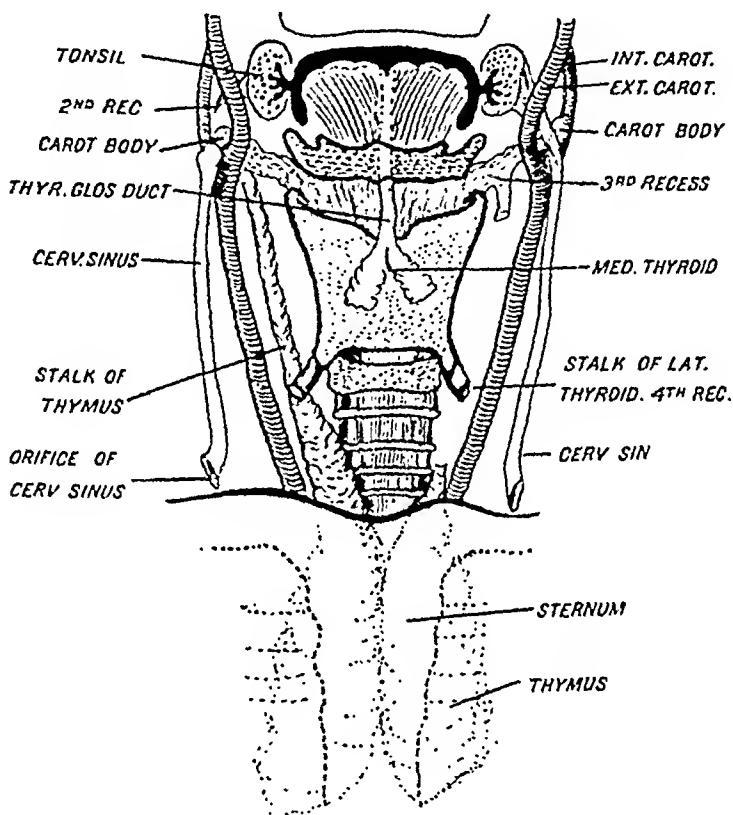


FIG. 299. Diagram to illustrate the various parts of the Visceral Recesses and Grooves which may persist. The 2nd recess gives rise to the tonsil; the recess may be in contact with an epithelial tube derived from the cervical sinus. The 3rd recess gives rise to the thymus and parathyroid III. The carotid body arises at the site of the 3rd recess, but its development has nothing to do with the recess.

external ear is suppressed. As already pointed out, remnants of the 2nd and 3rd clefts are included within the opening of the cervical sinus.

Within the *pharynx* traces of inner cleft recesses are to be seen besides the Eustachian opening (see Figs. 299, 312). The *tonsil* is developed in the lower or ventral part of the 2nd cleft; the anterior pillar of the fauces represents only the *position* of the 2nd arch. The *lateral recess of the pharynx* (fossa of Rosenmüller), behind the Eustachian tube, although sometimes regarded as a derivative of the 2nd cleft, is, as we have seen (p. 327), a secondary formation. The *pyriform fossa*, at each side of

an early stage in the development of the medullary plate of the head region results in a partial or complete suppression of the arch cartilages.

Nerves of the Visceral Arches (see Figs. 302, 303, 118).—The 3rd division of the Vth nerve is is, as has been already seen, the principal nerve of the 1st or mandibular arch. The nerve for the 2nd or hyoid arch is represented by the VIIth or facial. The nerve of the 3rd arch is the glosso-pharyngeal, that for the 4th is the superior laryngeal branch of the vagus, and for the 5th and 6th the inferior laryngeal (Fig. 303).

Each nerve of a visceral arch supplies (i) the muscles of the arch, (ii) the pharyngeal lining and cleft recess in front of the arch. The

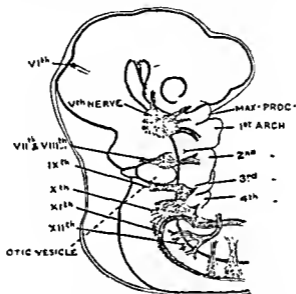


FIG 302 The Visceral Arches and their Nerves and Ganglia in a Human Embryo of the 5th week. (Streeter.)

chorda tympani and great superficial petrosal nerves represent the sensory and visceral branches of the facial to the 1st cleft.

The relationship of the nerves to the visceral arches is shown in Fig. 302, in a human embryo of 5 weeks. The position of these nerves in the adult is diagrammatically represented in Fig. 303. The Vth nerve and Gasserian ganglion are seen to lie at the base of the mandibular process. The ganglia of the VIIth and VIIIth nerves are placed at the base of the hyoid 2nd arch, in front of the otic vesicle, the fibres of the facial having already entered the arch. The glosso-pharyngeal and its ganglia lie behind the otic vesicle and at the base of the 3rd arch. The large ganglionic mass of the vagus lies over the bases of the 4th, 5th and 6th arches—or rather the tissue representing these arches. At this stage—the 5th week—the diffuse ganglion of the vagus and its issuing

Prof. Parsons [6] drew attention to the fact that there is a ridge of bone on the upper surface of the body of the hyoid, which may occasionally form an almost separate bar. It lies between the lesser horns, and appears to represent the copula or body of the 2nd arch. It may be separated from the body of the hyoid by a foramen. It will be seen later that the basal or pharyngeal part of the tongue arises from the floor of the pharynx in the field between the 2nd and 3rd arches, the 2nd arch providing most of the substance. The skeletal part of the hyoid arch suspends the tongue. There may be a process of bone from the

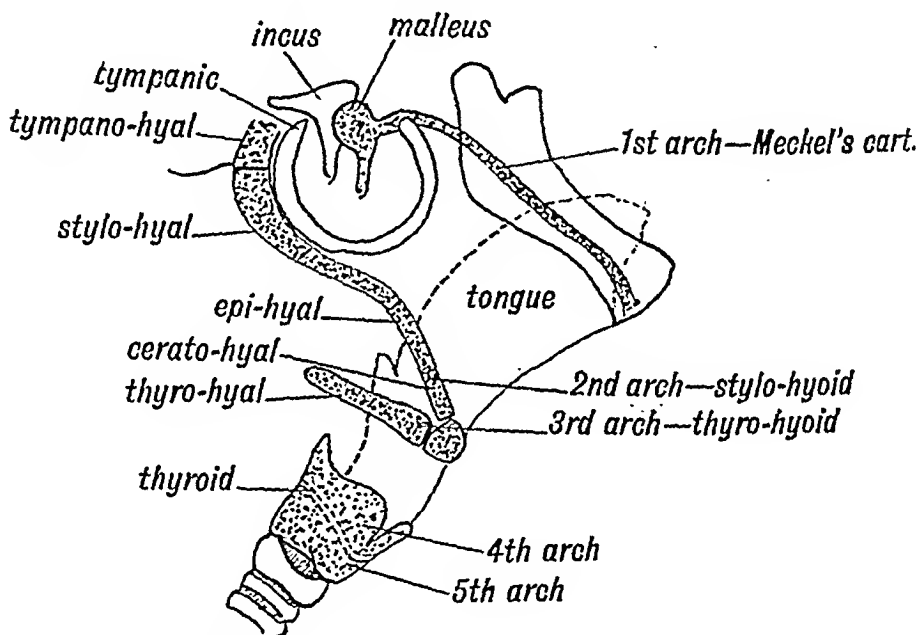


FIG. 301. Showing what becomes of the Cartilages of the Visceral Arches.

concavity of the body of the hyoid representing the hyolingual of lower vertebrates (Parsons).

The *great horn* of the hyoid represents the cartilage of the 3rd arch (Fig. 301). In the lowest mammals the cartilaginous bases of the 4th and 5th arches unite to form the thyroid cartilage, but in higher mammals, including man, this cartilage is made up entirely by the 4th arch [2]. The cartilages of the ultimate arches (5th and 6th) are probably represented by the cricoid, arytenoid and rings of the trachea (see also Fig. 440, p. 491). Even in mammals the cartilages of the last three branchial arches remain subservient to the purposes of respiration, just as in vertebrate animals in which these arches carry gills.

Mention has already been made of the peculiar part played by cells derived from the neural crest of the fore-brain in the development of the cartilaginous arches of the pharynx [7]. Damage to these cells at

an early stage in the development of the medullary plate of the head region results in a partial or complete suppression of the arch cartilages.

Nerves of the Visceral Arches (see Figs. 302, 303, 118).—The 3rd division of the Vth nerve is is, as has been already seen, the principal nerve of the 1st or mandibular arch. The nerve for the 2nd or hyoid arch is represented by the VIIth or facial. The nerve of the 3rd arch is the glosso-pharyngeal, that for the 4th is the superior laryngeal branch of the vagus, and for the 5th and 6th the inferior laryngeal (Fig. 303).

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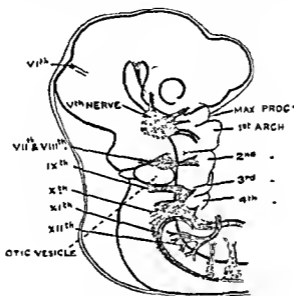


FIG 302 The Visceral Arches and their Nerves and Ganglia in a Human Embryo of the 5th week. (Streeter.)

chorda tympani and great superficial petrosal nerves represent the sensory and visceral branches of the facial to the 1st cleft.

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fibres rest on the dorsal wall of the pericardium, the heart being quite close to the source of its nerve fibres [8].

The spinal accessory nerve is to be regarded as an extension backwards of the vagal or branchial system to the cervical region of the cord. Its spinal fibres, which supply the sternomastoid and trapezius, both of branchial origin, arise from a prolongation of the dorso-motor nucleus of the vagus. The XIIth or hypoglossal nerve has primarily nothing to do with the branchial or visceral segments. The musculature of the

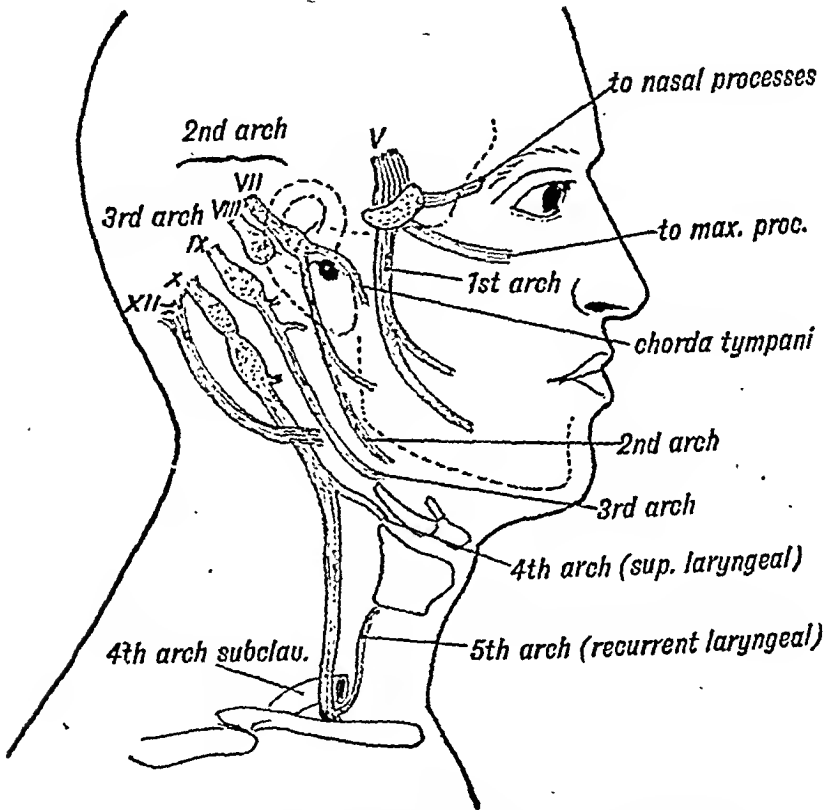


FIG. 303. Showing what becomes of the Nerves of the Visceral Arches.

tongue is derived from the last three occipital segments and is somatic in nature.

Epibranchial Placodes.—When the ganglia of the VIIth, IXth and Xth nerves begin to differentiate in the 5th week, they are in contact with the upper ends of their respective gill depressions—the 1st, 2nd and 3rd. An area of ectoderm at the upper end of each cleft depression becomes modified to form an epibranchial placode representing sense organs that are now lost in higher vertebrates (Fig. 298, A). During the 5th week these placodes are in contact with the ganglia just mentioned and the ganglion of the trunk of the vagus (ganglion nodosum) and of the trunk of the glosso-pharyngeal (ganglion petrosus) receive additions

from cells that are produced in, and migrate from, the placodes. The placodes become submerged during the formation of the cervical sinus, drawing down with them processes of the ectoderm [9].

Carotid Body.—Attached to the nerve of the 3rd arch (glossopharyngeal), and developed in connection with the artery of this arch, is the carotid body, a pressor-receptor mechanism concerned in the

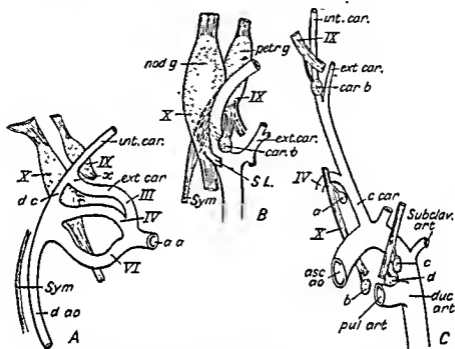


FIG. 304.

- A. The Aortic Arches (III, IV, V) of the right side of an embryo in the 6th week of development, showing the site at which the carotid body is developed. (This and accompanying Figures are after J. D. Boyd)

IX, X, Glossopharyngeal and vagal nerves with their trunk ganglia; x, site at which the carotid body is developed; ext. car., site at which external artery will arise; a o., aortic sac; d ao., dorsal aorta; d c., ductus caroticus; Sym, cervical sympathetic

- B. The same parts in the 7th week, the carotid body (car. b) being now defined. S.L., superior laryngeal; ext. car., external carotid.

- C. The Arch of the Aorta and Right Common Carotid (c. car.) of a foetus in the 9th week of development.

a, paraganglion near the origin of the right subclavian artery receiving depressor fibres from Xth; b, right aortic or suprascapular paraganglion; c, d, left aortic paraganglia, receiving fibres from the left vagus.

regulation of blood-pressure. Its development in the human embryo and foetus has been traced by Prof. J. D. Boyd [10]. By the end of the 9th week (Fig. 304, C) the body is seen to be applied to the antero-medial aspect of the internal carotid artery, immediately above the origin of the external carotid. Its afferent nerve twig comes from the IXth nerve. An earlier stage, that reached in the 7th week, is shown in Fig. 304, B. On the medial side of the internal carotid, at the site where the carotid body is developed, there are three masses of nerve

cells, namely, the ganglion of the trunk (or petrous) of the IXth, the corresponding ganglion of the Xth (nodose) and the superior ganglion of the sympathetic. Although the chief supply to the carotid body is from the IXth, it also receives nerve fibres from the two other masses. Later, cells from the sympathetic ganglion invade the body. In Fig. 304, *A*, a still earlier stage is shown, about the beginning of the 6th week. Towards the end of this week, at the site (*x*) indicated in the illustration, a ring or cuff of condensed tissue is formed in the superficial coat of the internal carotid artery, corresponding to the upper end of the 3rd aortic arch. The cells in the condensation are polyhedral in shape and have oval nuclei; they may be regarded as paraganglionic cells, but at no time do they yield a chromaffin reaction (Boyd). Presently, the condensed tissue becomes concentrated in the fork between the external and internal carotid arteries. The adjacent coat of the internal carotid artery becomes thinned and for a short time the lumen of the carotid is in communication with the paraganglionic tissue of the body, recalling a stage seen in the developing tadpole. Towards the end of the 2nd month, the carotid body separates from the coat of the internal carotid artery (Fig. 304, *C*).

Vascular bodies of a corresponding nature arise in all the arterial arches of the gills of the dog-fish and of other selachians. The mammalian carotid body has been evolved out of that of the 3rd (glossopharyngeal) arch. It is probable that the glomi or paraganglia depicted in Fig. 304, *C* (*a, b, c, d*) represent receptor bodies developed in connection with the 4th arch (subclavian) and 6th (pulmonary arch) of the selachian branchial system (Palme). That which is situated on the ascending part of the aortic arch, just above the origin of the left coronary artery, gives a chromaffin reaction.

Aortic Arches—the Arteries of the Visceral Arches.—In Fig. 293 is given the foetal arrangement of the aortic arches, and in Fig. 305 the vessels in the adult which are formed from them. The primitive ventral aorta (aortic sac) as it issues from the pericardium to enter the floor of the pharynx immediately breaks up into branches that enter the pharyngeal arches on the right and on the left. These branches form a right and left set, and as they represent the ventral aortae of fishes we may speak of them as the ventral aortic stems (see Fig. 294). From these stems arteries (aortic arches) pass upwards, one in each visceral arch, to terminate in the right and left *dorsal aortae*, which run backwards and become fused to form the descending thoracic aorta. The aortic arches are formed at a very early date. At the beginning of the 4th week the 1st or mandibular aortic arch has already made its transitory appearance; the 2nd (hyoid), 3rd, 4th, 5th and 6th appear in

succession, but by the 6th week, when the 6th or pulmonary arch [11] has appeared, the 1st and 2nd have atrophied (Fig. 304, A). Only for a brief period towards the end of the 5th week, when the embryo is about 5 mm. long, are all the arches open, and even then the 1st is atrophic while the 6th or pulmonary is developing. The 5th arch has only a transient existence. The aortic arches are formed by the union of a network of blood spaces that are developed within each visceral arch.

The 1st and 2nd aortic arches disappear; the 3rd remains as the first

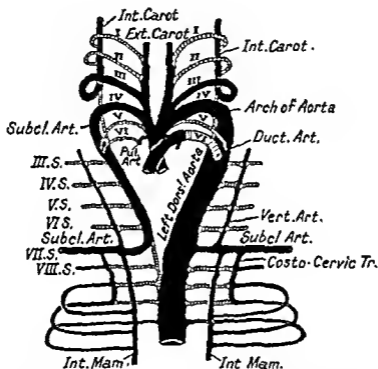


FIG. 305. A scheme of the Aortic Arches of the Human Embryo of the 5th week. The parts which disappear are shown lightly shaded. (After Broman.) III s, IV s, etc., segmental arteries, the outer part of the subclavian artery being derived from VII s.

part of the internal carotid, the 4th forms the 1st and 2nd stages of the right subclavian [12]. On the left side the 4th aortic arch forms that part of the arch of the aorta which lies between the origin of the left carotid and entrance of the ductus arteriosus (Fig. 305). The right and left 5th arch, or, to be more accurate, the 6th—for a transient arch appears between it and the 4th—gives off vessels to the lungs, which are developed in close connection with these arches [13]. This arch on the left side persists as part of the right pulmonary artery and ductus arteriosus (Fig. 307). On the right side the dorsal part disappears, the remaining segment joining in the formation of the right pulmonary artery. When

it is remembered that the 6th or pulmonary arch lies at the level of the larynx in the 5th week, and that, owing to the development of the neck, it has almost reached its final position in the 7th week, the rapid transformation of the parts in the region of the pharynx in the 2nd month will be realized. It is in this period that the hinder gill arches are buried and the cervical sinus formed and obliterated. It is during this descent that the dorsal aorta between the 3rd and 4th arches disappears (*ductus caroticus, d.c.*, Fig. 304, A).

Subclavian Arteries.—The visceral arches with their arteries are well developed before the limb-buds appear. When, at the end of the 4th week, these buds grow out to form the upper extremities, the artery

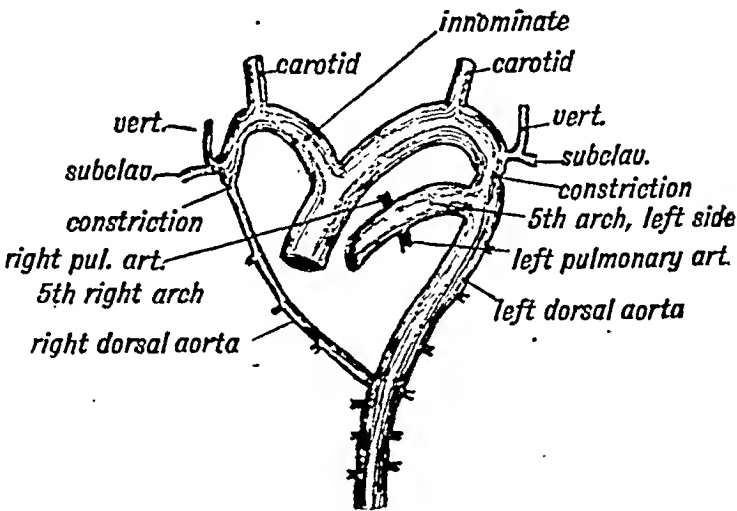


FIG. 306. The condition of the Right and Left Dorsal Aortae in a 7th-week Human Foetus. (After His.) The right arch and right dorsal aorta disappear beyond the origin of the right subclavian; a constriction may appear at the corresponding point on the left side.

that ultimately supplies each bud springs from the dorsal aorta and represents a dorsal segmental branch of that vessel. The embryonic or primitive subclavian is the artery of the 7th cervical segment, being situated at a considerable distance behind the 6th aortic arch. As the aortic arch-system is elongated to form the great vessels of the neck during the 6th and 7th weeks, the origin of the subclavian migrates forwards until it comes to lie opposite the 4th arch (Fig. 306). This artery forms the entire subclavian on the left side, but only that part beyond the origin of the vertebral on the right side [14].

Aortic Arch on the Right Side.—In birds it is the 4th right arch that forms the aortic arch, and this occasionally happens in man. In amphibians both the right and left 4th arches persist. The two dorsal aortae in which they end unite together, as they do in the human embryo, to form the descending thoracic aorta. The primitive subclavian arteries

spring from the dorsal aortae above the point where these two vessels fuse together. In the latter part of the 2nd month the short part of the right dorsal aorta, between the origin of the right subclavian artery and point of aortic fusion (7th dorsal vertebra) disappears, and then the subclavian artery appears as if it arose from the 4th right arch (Fig. 306). The communicating arterial twig, which is often seen uniting the superior intercostal artery of the right side with the artery of lower spaces, is formed by secondary anastomoses, and does not represent the right dorsal aorta [15].

Not unfrequently the right subclavian arises, not from the innominate, which represents the right ventral aortic stem, but as the last of the great branches which spring from the arch of the aorta. In such cases

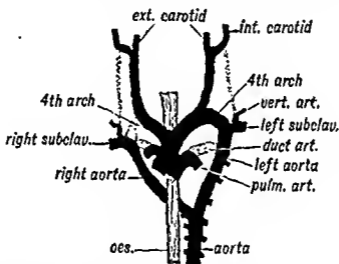


FIG. 307. Diagram showing the manner in which the Right Subclavian may arise as the last branch of the Arch of the Aorta. The parts of the aortic arch system which become obliterated are stippled.

two things have happened: (i) the 4th right aortic arch has been obliterated, (ii) the right dorsal aorta has persisted (Fig. 307).

Cases occur in which the permanent aorta is very much constricted at or near the point of entrance of the ductus arteriosus (see Fig. 306). It will be noticed that the corresponding part of the right dorsal aorta is obliterated. Such a constriction on the left side is to be regarded as corresponding to that on the right side, and indicates an attempt to produce a right aortic arch.

Dorsal Aortae.—It will be noticed that the parts of the dorsal aortae between the 3rd and 4th arches disappear (Fig. 307). The ventral aortae (aortic sac) give rise to the innominate and common carotid arteries, while the external carotid is a new formation (Fig. 301). With the marked elongation of the cervical region and the development of

the lungs in the 2nd month, the primitive position of the aortic arches is greatly disturbed. The heart, being the pump of the lungs, must accompany these organs. The ventral aortae become elongated into the common carotid and innominate arteries (Figs. 305, 307). The 4th aortic arch, which should lie opposite the upper part of the thyroid cartilage, comes to rest at the level of the 1st rib on the right side and within the thorax on the left, while the last aortic arch dragging the nerve of its segment in front of it (the recurrent laryngeal) comes to be situated within the thorax.

Muscles of the Visceral Arches.—Within each visceral arch a muscle plate is formed—the dorsal part recalling in its mode of appearance the muscle plate which develops in connection with each vertebral somite (see Fig. 180, p. 230). The muscles arising in each arch are supplied by the nerve of that arch; hence from the nerve supply alone one could infer the derivation of the musculature of the pharyngeal region. The muscles become differentiated in the latter part of the 2nd month. All the muscles supplied by the facial nerve—the platysma, muscles of expression, the stapedius, stylo-hyoid, posterior belly of the digastric, etc.—are derived from the muscle plate of the 2nd or hyoid arch. The muscles of mastication, with the tensors of the palate and tympanum, the anterior belly of the digastric and mylohyoid, are derived from the muscle segment of the mandibular arch. The stylopharyngeus, originally part of the constrictor, is derived from the 3rd arch. The musculature of the soft palate, including the levator palatae, and the constrictors of the pharynx are derived from the 3rd and 4th arches. The musculature of the larynx is developed out of that part of the constrictor sheet which formed the sphincter of the primitive oesophagus and may be assigned to the 2nd and 3rd branchial segments. From these same segments is derived the musculature of the sterno-mastoid and trapezius; hence their peculiar nerve supply [16].

Platysma and Muscles of the Face and Scalp.—The platysma myoides, the muscles of the face, scalp and external ear, are derived from the muscle plate of the 2nd or hyoid arch [17]. They are supplied with both motor and proprioceptive fibres by the facial, the nerve of this arch. The muscle bud, from which the whole platysma sheet is developed, is still confined to the area of the hyoid arch until the 7th week of development, when the bud spreads out in the subdermal tissues and forms a continuous muscular hood over the head and neck. To this hood or sheet, which is composed of two layers, a deep and superficial, the name of *platysma sheet* may be given. It is developed in the superficial fascia. During its expansion or migration the platysma sheet separates into three main divisions—a part for the neck—*platysma coli*; for the ear and

occiput—the occipito-auricular; and the facial division—for mouth, nose, orbits and forehead (Fig. 308). The muscles become differentiated during the 3rd month.

In man, the platysma sheet has undergone marked retrograde changes in the neck, scalp and external ear, but over the face it has become more highly specialized and differentiated than in any other animal [18]. From this sheet are derived the epicranial aponeurosis, the occipitalis and frontalis muscles. On the face the platysma sheet forms the muscles round the orbit, nose and mouth. The buccinator and levator anguli oris represent parts of the deeper layer of the sheet. The transversus

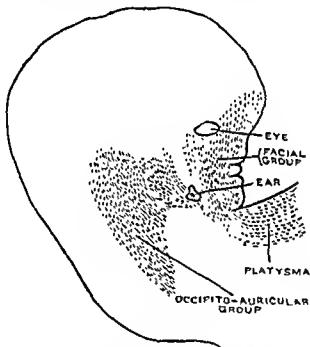


FIG. 308. The Expansion of the Platysma sheet in a Human Foetus of 7 weeks. (Futamura)

nuchae, fibres occasionally seen in man passing from the mid-dorsal line of the neck towards the ear and cheek, represent fibres constantly developed in lower primates and better still in rodents and carnivora as the *sphincter colli* and *sterno-facialis*.

The muscles supplied by the facial nerve are peculiar in that they are the physical basis into which many mental states are reflected and in which they are realized. Through them mental conditions are manifested. It is found that the differentiation of this sheet into well-marked and separate muscles proceeds *pari passu* with the development of the brain. The more highly convoluted the brain of any primate, and the more massive its basal ganglia, then the more highly specialized

are its facial muscles. It is remarkable that the sheet should arise from a visceral arch which originally was closely connected with the function of respiration. To some extent the platysma does come into action during forced respiration even in man.

The Neck.—If the reader will turn to Fig. 59 it will be seen that the head becomes demarcated from the trunk and a neck comes into existence in the human embryo during the 7th and 8th weeks of development. It is during these weeks that the fish-like organization of the embryonic pharynx becomes replaced by one which is mammalian. Although the seven cervical somites are demarcated early in the 4th week of development, the head is so flexed upon the trunk that the mandible is in contact with the pericardium. The neck comes into existence by the production and growth of tissues between the mandibular arch and pericardium, this growth in the ventral aspect of the cervical region being accompanied by an extension or elevation of the head. The heart itself is anchored to the roots of the developing lungs; all the tissues—nerves, vessels, muscles, air and food passages—passing from the head to the region of the thorax are elongated during this movement.

NOTES AND REFERENCES

[1] I have refrained from using the term "branchial" as names for the arches of the embryonic pharynx. As far as is convenient I speak of the first arch as the mandibular, the second as the hyoid, the third, which is the first true branchial, as the glosso-pharyngeal, and the others as vagal arches.

[2] For the evolution and morphology of the pharyngeal muscles, see *The Cranial Muscles of Vertebrates* (1936), by the late Prof. F. H. Edgeworth.

[3] For Prof. J. E. Frazer's account of the cervical sinus, see *Brit. Jour. Surg.*, 1923, 2, 131; *Jour. Anat.*, 1927, 61, 133; *Manual of Embryology*, 1940.

[4] For malformations of pharynx and neck, see Keith, Sir A., *Brit. Med. Jour.*, 1909, 2, 310, 363, 438.

[5] For an account of the skeletal elements of the pharynx, see De Beer, G. R., note [1], Chapter XII; Edgeworth, F. H., preceding note [2]; Frasin, I., *Ann. d'Anat. Path.*, 1937, 14, 443.

[6] Parsons, F. G., *Jour. Anat.*, 1909, 43, 270.

[7] See Chapter IV, p. 75, note [25]; Chapter XIII, p. 263, note [5].

[8] For general literature on the nerves of the pharynx, see Ariens Kappers, note [3], Chapter IX. Some of the more recent papers are: Shaner, R., *Jour. Anat.*, 1934, 68, 314 (motor nuclei of cranial nerves of pig); Woodburne, R. T., *Jour. Comp. Neur.*, 1936, 65, 403 (Vth nerve); Frade, F., *Arch. Biol.*, 1938, 49, 617 (origin of Gasserian ganglion); Wakeley and Edgeworth, *Jour. Anat.*, 1933, 67, 420 (afferent fibres of Vth and VIIth); Waddell, G., *ibid.*, 1938, 67, 175 (taste fibres in VIIth); Schimert, J., *Zeitsch. Mik. Anat. Forsch.*, 1936, 39, (VIIth nerve); Wakeley, C. P. G., *Lancet*, 1939, 1, 749; Ransom and Others, *Amer. Jour. Anat.*, 1933, 53, 289 (composition of Xth); Jones, R. L., *Jour. Comp. Neur.*, 1937, 67, 469 (nodose ganglion); Pearson, A. A., *ibid.*, 1938, 68, 243 (Xith in human embryo); Romanes, G. J., *Jour. Anat.*, 1940, 74, 336 (Xith in sheep); Downman, C. B. B., *ibid.*, 1939, 73, 387 (XIIth nerve).

[9] Frazer, J. E., *Jour. Anat.*, 1927, 61, 133; Campenhou, E. van, *Archiv. Biol.*, 1936, 47, 585.

[10] For recent literature on the carotid body and similar structures, see Boyd, J. D., *Contrib. Emb.*, 1937, 26, 3; *Jour. Anat.*, 1936, 71, 157 (in selachians); *Anat. Anz.*, 1937, 84, 387 (nerve supply); *Jour. Anat.*, 1942, 76, 248 (reptilian form); Sheehan and Others, *Anat. Rec.*, 1941, 80, 431 (nerve supply); Hammond, W. S., *Amer. Jour. Anat.*, 1942, 69, 265 (development of aortic bodies in cat); Nonidez, J., *ibid.*, 1941, 68, 151 (aortic receptor bodies); Hollinshead, W. H., *Anat. Rec.*, 1942, 84, 1 (comparison of carotid body with the coceygeal glomus); Goormaghtigh, N., *Jour. Anat.*, 1936, 71, 76; Stoehr, Ph., *Ergeb. Anat. Entwickl.*, 1938, 32, 1.

[11] Reagan, F., *Amer. Jour. Anat.*, 1911, 12, 493; Shaner, R. F., *ibid.*, 1921, 29, 407.

[12] The literature on the development and abnormalities of the aortic arches is too voluminous to be given here. Some of the chief recent papers are: Woollard, H. H., *Contrib. Emb.*, 1922, 22, 139; Congdon, E. D., *ibid.*, 1922, 20, 51; Cairney, J., *Jour. Anat.*, 1925, 59, 265; Windle, W. F., *ibid.*, 1928, 62, 518; Lockhart, R. D., *ibid.*, 1930, 64, 189 (right and left aortic arches); Golub, D. M., *Zeitschr. Anat. Entwickl.*, 1929, 90, 690 (5th aortic arch in embryo). For variations in the origin of stems from the aortic arch, see Williams and Edmonds, *Anat. Rec.*, 1935, 62, 139; De Garis, C. F., *Jour. Anat.*, 1936, 70, 149; *Anat. Rec.*, 1938, 70, 251 (variations in arch of rhesus monkey).

[13] Ingalls, N. W., *Anat. Rec.*, 1932, 53, 269 (pulmonary arteries arising from aorta).

[15] See references given in notes [12], [14].

[16] Edgeworth, F. H., see note [2].

[17] Futamura, R., *Anat. Hefte*, 1907, 32, 479.

[18] For evolution of facial musculature, see Huber, E., *The Evolution of the Facial Musculature*, 1931; Burkitt and Lightoller, *Jour. Anat.*, 1928, 62, 33; Lightoller, G. S., *ibid.*, 1940, 74, 390; *ibid.*, 1942, 76, 258.

CHAPTER XIX

TONGUE, THYROID AND STRUCTURES DEVELOPED FROM THE WALLS OF THE PRIMITIVE PHARYNX

The Tongue and its Development.—Two parts are to be recognized in the tongue. The *buccal part* (Fig. 309) is situated in front of the foramen caecum and the V-shaped groove. It is covered by papillae, concerned in mastication and liable to cancer. The second or *pharyngeal part*, directed towards the hinder wall of the pharynx (Fig. 309), is covered by glandular and lymphoid tissue and concerned with swallowing. These

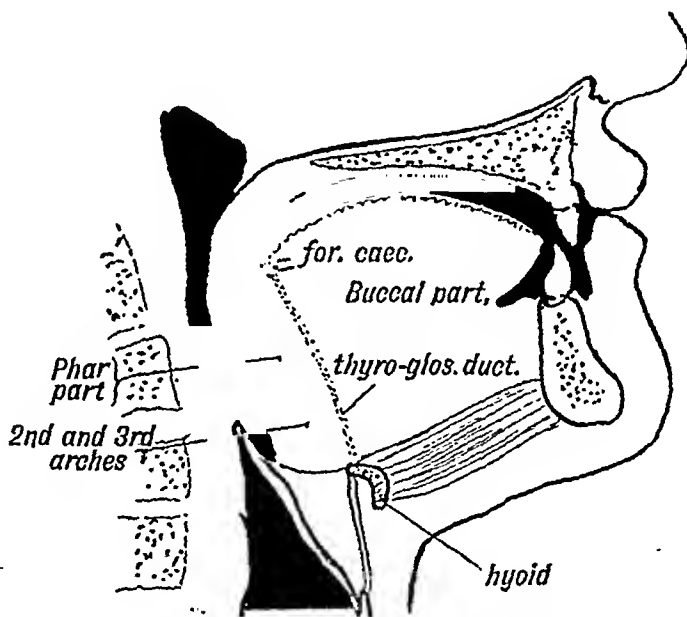


FIG. 309. Showing the Buccal and Pharyngeal Parts of the Tongue.

two parts are not only different in function but also in origin and development.

The *buccal part* arises during the 5th week by an upgrowth—the *tuberculum impar*—that springs from the floor of the pharynx, in the groove between the mandibular and hyoid arches (Fig. 296). This outgrowth was at one time believed to give rise to the whole of the buccal part of the tongue, but researches made by Kallius and others [1] have demonstrated that in the 6th week there arise from the mandibular arch, on each side of the tuberculum impar, right and left lingual buds which fuse with and bury the median element (Fig. 310). Hence the buccal

part of the tongue is bilateral in origin, and as its nerve supply shows, is essentially a product of the mandibular arch. In the 7th week the tip of the tongue is bifid, because the lateral buds are imperfectly fused (Paulet). The bilateral origin of the tongue explains the occasional occurrence of a bifid tip and the formation of cysts in the median raphe. Besides the lingual nerve, the chorda-tympani—the branch of the facial nerve which enters the mandibular arch—also supplies the buccal parts with sensory (taste) fibres. Until the 7th week the buccal part of the tongue is still separated from the pharyngeal part by a depression in the floor of the pharynx. The buccal part, however, remains still unseparated from the mandibular arch. There then occurs a down-

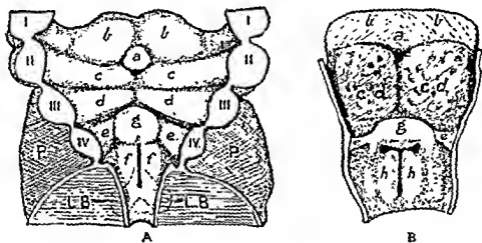


FIG. 310.

- A Parts which go to the formation of the Tongue, as seen in the floor of the Pharynx of a Human Embryo, early in the 6th week. (After Prof. Frazer.) *a*, tubercle impar; *b, b*, mandibular lingual elements; *c, c*, hyoid elements; *d, d*, 3rd arch or glosso-pharyngeal element; *e, e*, 4th arch; *f*, epiglottis or furcula; *f, f*, laryngeal folds; *P, P*, pericardium; *L.B., L.B.*, lung buds.
- B The Human Tongue, seen from behind at the 9th week of development. *a, b*, aryteno-epiglottidean folds. The other letters indicate parts shown in the adjoining figure.

growth of epithelium in the form of a horse-shoe plate, which separates the lingual from the mandibular tissues; in this way the tongue becomes separated from the alveolar ridge of the mandible. In the floor space between the tongue and mandible are developed the submaxillary and sublingual glands. Not unfrequently part of this glandular field may be imperfectly separated from the tongue, and in this manner various peculiar congenital malformations of the tongue are produced (see Fig. 311).

The pharyngeal part of the tongue is derived chiefly from the hyoid arch, but an addition is also made from the 3rd (glosso-pharyngeal) arch. The hyoid bone is formed in both 2nd and 3rd arches. The glosso-pharyngeal, the nerve of the 3rd arch, or more strictly of the 2nd

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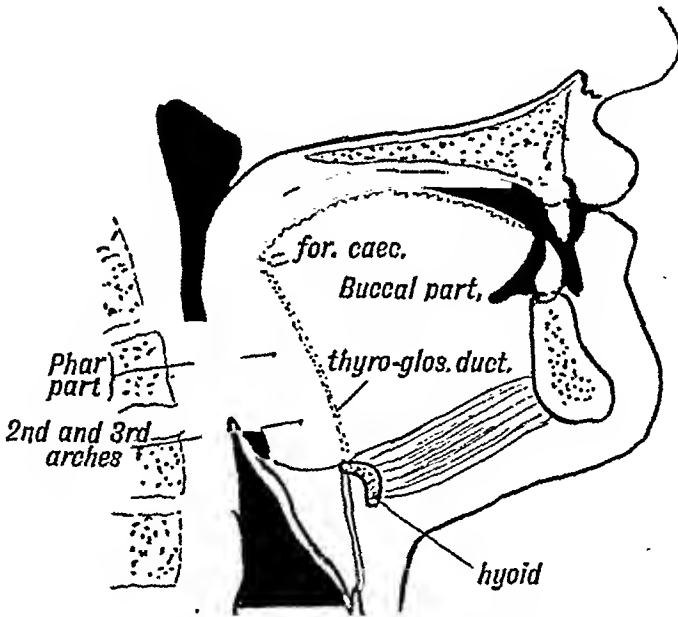


FIG. 309. Showing the Buccal and Pharyngeal Parts of the Tongue.

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cleft (Fig. 312) to its place in the floor of the mouth. The sense of taste is present in a child born at the 8th month of development [3].

Lingual Papillae.—The filiform papillae are the first to appear (9th week), then the fungiform, a few of which, along the posterior border of the buccal part, become enlarged and sink to form circumvallate papillae, round the bases of which taste buds are developed. The papillae are confined to the buccal or masticatory part of the tongue. Fungiform papillae develop over terminals of the lingual nerve, while the taste buds of the circumvallate papillae arise over terminals of the IXth nerve. It will be observed that the taste papillae are situated at the brink of the pharynx (Fig. 309), at which the food is seized and carried away by involuntary muscles. At the lateral margins of the buccal part of the tongue, just in front of the anterior pillars of the fauces, the

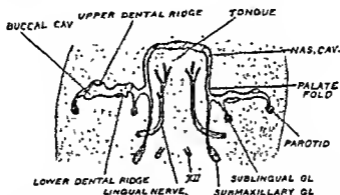


FIG 312 Showing the Origin of the Submaxillary and Sublingual Glands from furrows between the gum and tongue during the 7th week. The tongue projects between the maxillary folds into the nasal cavity. (After His.)

fungiform papillae are arranged in a series of laminae, recalling and corresponding to the *papillae foliatae* of low primates and of rodents. Between the *papillae foliatae* occur taste buds [3]. On the under surface of the tongue at birth, on each side of the sublingual papillae and over the position of the ranine artery, are two fimbriated folds of mucous membrane, the *pliae fimbriatae*, structures which are well developed in lemurs, serving as tooth-combs (Wood-Jones [4]). A remnant of the *pliae fimbriatae* can commonly be seen on the under surface of the human tongue.

Epiglottis.—The origin of the larynx, trachea, bronchi and lungs as a depression and bud from the floor of the pharynx will be dealt with later (p. 490); but the origin during the 5th week of the furcula (Fig. 296), a process from which the epiglottis is derived, may be noted here. The furcula, and consequently the epiglottis, arise from elements contributed by both 3rd and 4th arches (Fig. 310, B). The thyroid cartilage arises

cleft, supplies it. The V-shaped groove (sulcus terminalis) marks the union of the buccal with the basal or pharyngeal part. The foramen caecum, at the apex of the V-shaped fissure, marks the site from which the thyroid outgrowth took place (Fig. 311). It is of interest to note that while the various elements are uniting in the floor of the mouth to form the tongue, nasal and maxillary elements are uniting in its roof to form the palate.

Musculature of the Tongue.—The muscles of the tongue, which make up almost its entire substance, do not arise within the visceral arches, but are of extraneous origin, arising from the muscle plates of the three

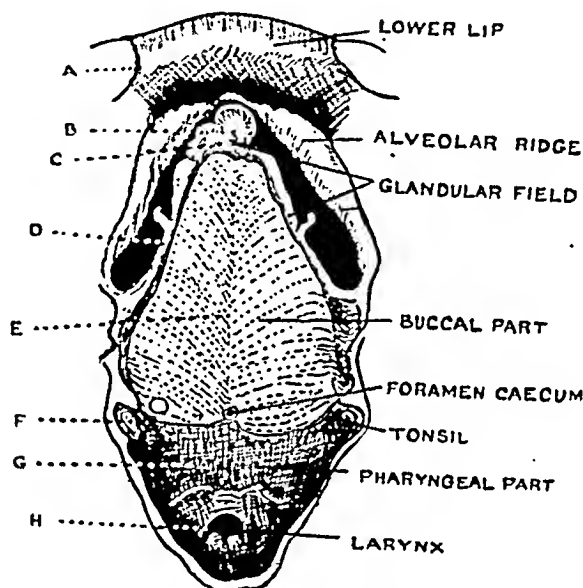


FIG. 311. Upper Surface of the Tongue of a Child in which the glandular tissue which forms the sublingual and submaxillary glands has been imperfectly separated from the tongue by the down-growth of the mandibulo-lingual plate of epithelium. A, lower lip; B, alveolar ridge; C, glandular tissue (sublingual); D, submaxillary; E, buccal part of tongue; F, tonsil; G, pharyngeal part of tongue; H, opening of larynx.

posterior or occipital segments of the head. The occipital buds migrate forwards along the lower border of the triangular field of the neck (Fig. 298, A), thus reaching the floor of the pharynx. Hence, while the sensory nerves of the tongue come from the nerves of the 1st, 2nd and 3rd visceral arches, its motor fibres (hypoglossal) are derived from the posterior cephalic segments. The primitive muscle of the tongue is the genio-hyoid; the genio-glossus is a derivative of it, and so is the hyo-glossus. The lingual muscles are already recognizable in the 6th week, but the intrinsic muscles of the tongue, which have so much to do with its finer movements, are later in point of differentiation—appearing late in the 2nd month [2]. As the intrinsic muscles form, the tongue widens and descends from its position within the palatal

invasion then spreads across the roof of the pharynx to the lateral recesses (Fig. 314). After birth lymphoid follicles form in the anterior

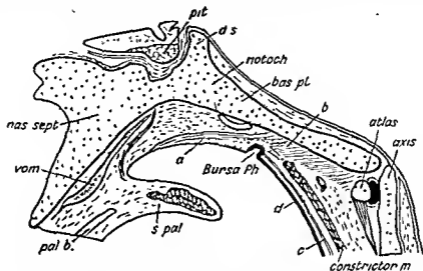


FIG 313 Sagittal section of the Naso-Pharynx of a Foetus of 10 weeks. (T. Snook.) a, Fascia pharyngeobasilaris; b, median fibrous raphe; c, pharyngeal aponeurosis; d, mucous membrane; ds, dorsum sellae. A section of the soft palate (s, pal) with the palatal muscles. The pituitary (pit.) and adjacent parts of the brain.

and lateral lips of the bursa, recalling in appearance the vulval structures of the infant. The bursa is occasionally absent, but the tonsillar tissue

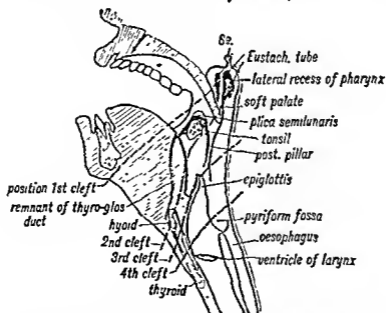


FIG 314. Showing the position of the Visceral Clefts in the Adult. The lines only indicate the approximate positions of the clefts. For instance, the soft palate is made up largely from the 3rd arch. See median pharyngeal recess or bursa.

is always developed. The latter often becomes pathologically overgrown, giving rise to adenoids. The pharyngeal tonsil, with the palatal

from the 4th arch. The superior laryngeal is the nerve of the 4th arch, hence it supplies the epiglottis and upper part of the larynx. The epiglottis and palate are peculiar to mammals. They separate the respiratory passage from the mouth. In all mammals the epiglottis lies within the nasopharynx in contact with the soft palate, but with the acquisition of speech in man this relationship is lost [5].

Origin of the Salivary Glands.—In the depression between the tongue and the mandible, formed by the opening out of the linguo-mandibular plate of epithelium, there appear two linear furrows (Fig. 312). From the inner or mesial of these two furrows arises the submaxillary gland; from the outer or lateral, at a rather later date (7th week), grows the sublingual [6]. While the latter arises by a series of buds from the endodermal lining of the groove, the former—the submaxillary—is developed by the enclosure of the endodermal furrow, which later becomes canaliculized and opens as a duct at the sublingual papilla, while the gland itself arises by a process of budding from the distal end of the enclosed endodermal cord. The submaxillary ganglion is made up of nerve cells which migrate from the geniculate ganglion during the outgrowth of the chorda tympani. The *parotid gland*, which is the first of the salivary glands to be developed (6th week), springs as a bud of ectoderm from the lateral or bucco-alveolar recess of the primitive mouth (Fig. 312). Its duct appears first as a groove, which later becomes enclosed to form a canal [7]. The gland grows backwards in the connective tissue over the masseter, and at birth is comparatively superficial in position, but as the mandible and external auditory process grow, it sinks inwards to surround the styloid process, pushing the deep cervical fascia beneath it. In this way the stylo-mandibular ligament is formed from the fascia pushed in front of it. Its nerves are derived from the 3rd division of the Vth (auriculo-temporal). Salivary glands are accessory to the function of mastication, and hence are developed only in mammals.

Pharyngeal Tonsil [8].—A sagittal section of the head of a foetus in the 10th week of development (Fig. 313) reveals in the roof of the pharynx, under the basilar plate of the spheno-occipital, a median recess or bursa of the mucous membrane. The bursa is surrounded by submucous tissue and in its vicinity are three structures (Fig. 313), namely, a remnant of the notochord (*notoch.*), the basilar fascia (*a*), and the fibrous tissue of the median raphe (*b*). In the submucous tissue, in front of and on each side of the bursa, reticular tissue has been differentiated; it is richly supplied with vessels. At the end of the 3rd month lymph vessels invade the reticular tissue and lymphocytes accumulate in front of and on each side of the bursa. The lymphocytic

invasion then spreads across the roof of the pharynx to the lateral recesses (Fig. 314). After birth lymphoid follicles form in the anterior

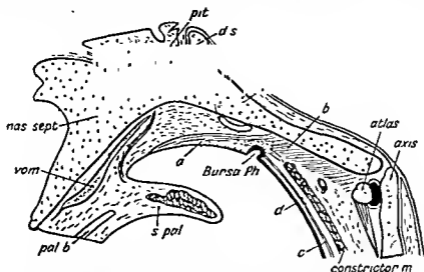


FIG. 313. Sagittal section of the Naso-Pharynx of a Fœtus of 10 weeks. (T. Snook.) *a*, Fascia pharyngeobasilaris; *b*, median fibrous raphe; *c*, pharyngeal aponeurosis; *d*, mucous membrane; *ds*, dorsum sellae. A section of the soft palate (*s. pal*) with the palatal muscles. The pituitary (*pit.*) and adjacent parts of the brain.

and lateral lips of the bursa, recalling in appearance the vulval structures of the infant. The bursa is occasionally absent, but the tonsillar tissue

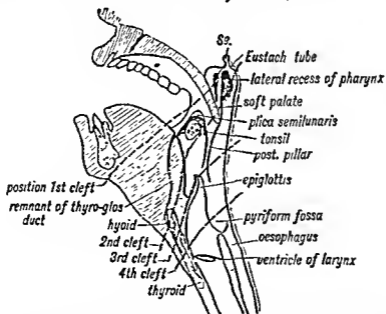


FIG. 314. Showing the position of the Visceral Clefts in the Adult. The lines only indicate the approximate positions of the clefts. For instance, the soft palate is made up largely from the 3rd arch. See median pharyngeal recess or bursa.

is always developed. The latter often becomes pathologically overgrown, giving rise to adenoids. The pharyngeal tonsil, with the palatal

tonsil and the lymphoid tissue on the basal aspect of the tongue, form a circum-pharyngeal ring. The functional significance of tonsillar tissue is still uncertain.

Before proceeding to trace the development of the tonsil and other glandular structures that arise from the endoderm of the embryonic pharynx, it may be well to glance at the interior of the adult pharynx (Fig. 314) and note how far the embryonic arches and recesses can be recognized. The position of the 1st cleft is shown passing behind the mandibular symphysis to the opening of the Eustachian tube; the 2nd is made to cross the tonsillar recess, indicating that the tonsil is a product of the 2nd cleft. We have seen (p. 327) that the dorsal end of the 2nd (hyoid) arch and the corresponding parts of the 1st and 2nd clefts are carried into the Eustachian recess. The soft palate, as it forms, crosses the 1st and 2nd clefts. The anterior pillar of the tonsillar recess contains the palato-glossal muscle, an up-growth from the tongue, while the posterior pillar contains the palato-pharyngeus, an up-growth from the constrictor muscles (products of the 3rd and 4th arches). Nevertheless, the tonsillar pocket represents part of the 2nd cleft recess. The 3rd cleft recess, from which the thymus takes its origin, is seen to pass behind the body of the hyoid and in front of the epiglottis, to end on the side of the pharynx. The 4th cleft, which occasionally gives rise to thyroid tissue, crosses the pyriform fossa.

The Tonsil.—The tonsil arises early in the 3rd month of foetal life from the ventral part of the 2nd cleft recess which is left between the soft palate and the tongue (Fig. 317, *B*). In the 4th month eight or ten isolated buds of endoderm push out from an elevation or tubercle situated in this recess or pocket, and grow into the mesodermal tissue in the wall of the pharynx (Fig. 316). The buds afterwards canaliculize and form the crypts and glandular tissue of the tonsil. Follicles of lymphoid tissue—for the tonsil must be regarded as a lymphoid structure—begin to collect round these glandular buds in the 5th month of foetal life. After birth the crypts, one after another, lose their openings; their epithelium becomes invaded by lymphocytes and thus nodules of lymphoid tissue are formed [9].

Concerning the origin of the lymphoid cells, both of the tonsil and the thymus, there are two quite distinct theories. The more recent (Gul-land's) is, that the epithelial endodermal cells, which form the glandular buds of the tonsil, give rise to broods of lymphoid cells; the older and the better founded, that these lymphoid cells arise from the blood or surrounding connective tissue, creep in and form follicles round the glandular endodermal buds. It now seems more likely that the endoderm of the 2nd cleft (tonsillar), like that of the 3rd cleft (thymic), has

the power of causing the mesoderm it comes in contact with to produce or to harbour lymphocytes [10].

A fold of mucous membrane, the *plica triangularis* (Fig. 315), passes from the lower part of the tonsil to the anterior pillar of the fauces. It represents the anterior part of the elevation or tubercle in which the glandular buds develop. Although present in the foetus, it commonly disappears in the adult. Its attachment to the tonsil marks a line of separation between an anterior and posterior group of tonsillar outgrowths (Fig. 316). The recess above the tonsil, sometimes crossed by a fold—the *plica semilunaris*—is a remnant of the recess of the 2nd cleft in which the tonsil is developed (Fig. 315). In many mammals the tonsillar recess assumes the form of a funnel-like process resembling

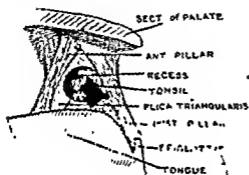


FIG. 315.

FIG. 315. The Tonsil in a Human Foetus of 8 months (Brit and Butterfield.)

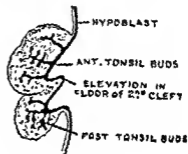


FIG. 316.

FIG. 316. Section across the 2nd cleft recess showing the Outgrowth of the Tonsillar Buds. The elevation between the anterior and posterior groups forms the lower part of the *plica triangularis*. (After Hammar.)

the finger of a glove, the blind end reaching almost to the angle of the jaw.

The tonsil is part of a great lymphoid system stationed along the alimentary canal. It reaches its fullest growth in youth, as is the case with the lymphoid system generally; when active growth of the system is over, and especially in the years of decay, it becomes markedly reduced in size. Occasionally the tonsillar recess projects outwards, and comes in contact with a tubular fistula representing the cervical sinus (see Fig. 299).

Lingual Tonsil.—That part of the tongue (pharyngeal) produced from the 2nd and 3rd arches is studded with mucous glands. The glands are surrounded by nodules of lymphoid tissue—the collective glandular mass receiving the name of lingual tonsil.

The Thymus.—The thymus arises in the same manner as the tonsil, only from the 3rd instead of the 2nd cleft (Fig. 317). The position of the inner recess of the 3rd cleft is represented in the adult by a space in

front, and on each side, of the epiglottis. It is crossed by the posterior pillars of the fauces, which represent a continuation of the palatal processes (Fig. 314). In the 6th week the 3rd pharyngeal pocket has assumed the form shown diagrammatically in Fig. 317, *B*, where its lower and hinder wall is represented as a flask-like process, lined by thickened endoderm, the embryological basis of the thymus [11]. On the dorsal part of the same pocket there is another thickening representing the lower *parathyroid* or epithelial body, while the original

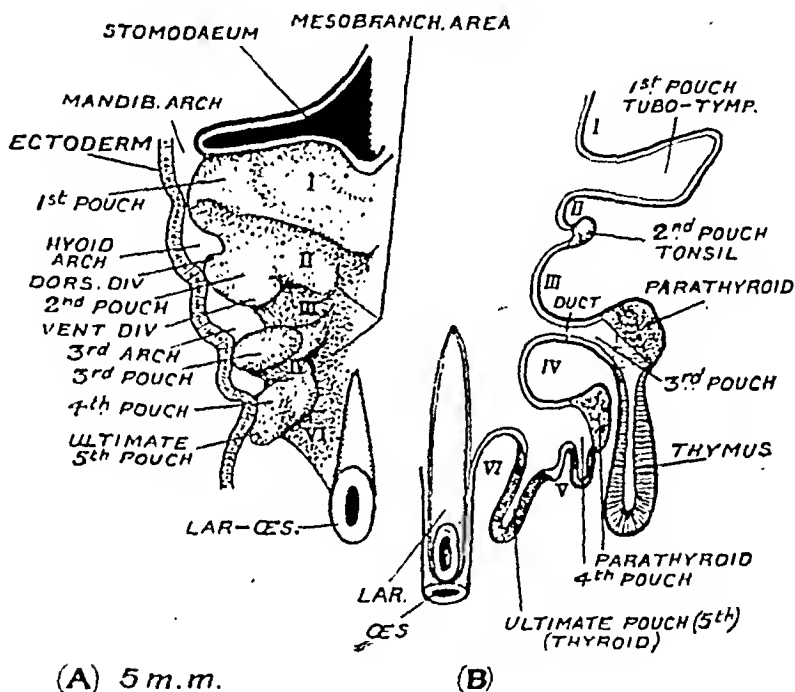


FIG. 317.

- A. The Lining Membrane of the Pharynx of a Human Embryo, 5 mm. long (5 weeks old), seen on its ventral aspect and showing the external configuration and relationships of the pharyngeal pockets. (After Grosser.)
- B. A schematic representation of the pharyngeal pockets and the glandular structures rising from them in the 6th week of development. (After Grosser.)

mouth of the pocket has been drawn out to form a tubular process or duct. In Fig. 317, *A*, is represented another view of the 3rd pocket, during the 5th week of development. By the 7th week the ectodermal covering, shown in Fig. 317, *A*, has been invaginated to form the cervical sinus and vesicle, the latter being continuous with the thymic outgrowth (see Fig. 297). The neck of the glandular thymic pocket becomes separated from the pharynx in the 7th week and usually disappears, but a strand of tissue frequently persists and represents the stalk of the outgrowth (Fig. 319). It is held by some embryologists that the ectoderm of the cervical sinus makes a large contribution to the thymic bud, forming its cortical zone [11]. By a species of secondary budding the

thymic tissue becomes broken up into islands or separated acini. The epithelial acini proliferate and give rise to a meshwork of united cells (syncytium), in which hroods of lymphocytes appear in the cortical zone during the 3rd month. The lymphoid cells become aggregated into follicles where the production of lymphocytes is continued. The medulla, which is certainly of endodermal origin, is made up of cyto-reticular tissue. The concentric bodies, known as the corpuscles of Hassall, [12] were at one time regarded as remnants of the endoderm, but are now generally regarded as structures derived from mesoderm that surrounds the cortex and forms a capsular covering for the developing thymus. The endothelial cells lining segments of the degenerating

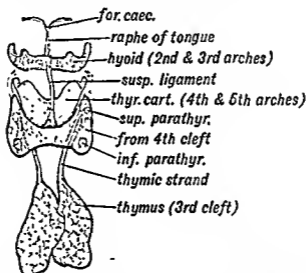


FIG. 318. Diagram of the Thyroid and Thymus. The position of the parathyroids on the posterior aspect of the lateral lobes of the thyroid is indicated.

capillaries may proliferate, occlude the lumen, and thus give rise to a Hassall's corpuscle (see also p. 471). It is estimated that the thymus of a child at birth contains over a million corpuscles. The lateral lobes come together under the ventral aortae and pericardium during the 7th week, and ultimately assume a thoracic position along with these structures. The pointed upper extremity of each lateral lobe can be traced upwards in the fully developed foetus, under the lateral lobes of the thyroid towards the thyro-hyoid membrane (Figs. 299, 318). These apical strands represent the stalk of the thymic buds. Thymus buds may occasionally arise from the 4th pouch (Fig. 317, B), and possibly from the cervical sinus [11].

As we are ignorant of the part played by lymphocytes in the economy of the living body, we can offer no satisfactory explanation of the purpose served by the thymus. The thymic epithelium appears to

have the power of compelling the mesoderm it invades to become lymphoid in nature [13].

The thymus reaches its fullest growth in early childhood (3rd or 4th year), and continues large as long as the body is in a state of active growth. It begins to shrivel up when maturity is reached, and only a remnant is left as a rule, less remaining in men than in women [14]. It receives its blood supply from the 4th aortic arches through the internal mammary. In manner of origin it resembles the tonsil; indeed, it may be regarded as a buried tonsil. There is a profuse production of lymphoid cells in the gill clefts of fishes, many of which wander out, and by their phagocytic properties help to keep the gill surfaces clean. This fact throws some light on the origin of so much lymphoid tissue from the 2nd and 3rd cleft recesses in higher animals.

The Thyroid [15].—The site at which the thyroid gland arises is shown in Fig. 296, p. 346—on the floor of the pharynx behind the tuberculum impar and exactly in the middle line. The endoderm of the retro-mandibular groove gives rise to a saccular diverticulum almost as soon as the fore-gut becomes differentiated—early in the 4th week of development. Indeed, it is the first of all glandular structures to be differentiated. Immediately in front of the thyroid evagination arises the buccal part of the tongue; behind it is produced the pharyngeal part. The foramen caecum in the sulcus terminalis marks the site at which the thyroid evagination began (Fig. 310, *B*). The endodermal vesicle thus formed grows downwards and backwards through the tissue in which the body of the hyoid will be formed, and as it extends, bifurcates. The stalk of the evagination, at first hollow, apparently represents a duct. The stalk quickly becomes solid, breaks up and by the 6th week has disappeared. The epithelium of the main body of the out-growth proliferates, and in the 7th week forms a transverse plate ventral to the larynx (Fig. 297). The plate is invaded and broken up into reticulating columns by the surrounding mesoderm. In the 3rd month the epithelial cells become arranged as follicles; these at a later date are converted into vesicles. The original plate assumes a bent or horse-shoe form, the middle part forming the isthmus, the side parts the lateral lobes (Figs. 318, 319).

When the median thyroid bud reaches the region of the larynx and spreads right and left to form lateral extensions, these extensions or lobes come into contact with the buds that are produced from the 4th pharyngeal recesses (Fig. 317). From these arise thyroid tissue and also the upper pair of parathyroids (Fig. 317). Both thyroid and parathyroid become applied to the dorsal aspect of the lateral lobes of the median thyroid (Fig. 319)—the larger part of each lateral lobe being

the product of the median bud. As will be seen from Fig. 317, *B*, the 4th pharyngeal recess is complex in its nature, including a representative of the 5th recess, known as the ultimo-branchial body. It is this latter element that gives rise to the lateral buds of the thyroid.

The thyroid is present in all vertebrates and, although it arises in a manner which suggests that at one time it was a gland of the mouth, yet in no animal does a functional duct persist. Its early origin in the embryo and its universal distribution in vertebrates point to the antiquity and importance of its function. We now suspect that all glandular structures had originally a double function, producing both external and internal secretions. It is reasonable to suppose that, as regards the thyroid, its excretory function has been lost. Vesicles contain colloid as early as the 3rd month and are apparently then functional [16]. It is a suggestive

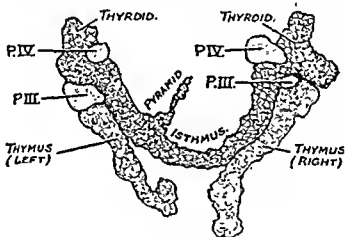


FIG. 318. THE THYROID GLAND AND ITS ASSOCIATED STRUCTURES.

fact that in amphibia the thyroid is suspended within one of the great lymphatic sinuses of the neck [17].

Thyro-glossal Duct.—In the great majority of human subjects the thyro-glossal duct or stalk completely disappears at the commencement of the 2nd month of development; the foramen caecum marks one extremity, while a ligament or a *pyramid* of thyroid tissue prolonging the isthmus towards the hyoid bone often marks the other extremity (Fig. 318). The *pyramid of the isthmus* may carry on it a detached part of the thyro-hyoid muscle—the *levator glandulae thyroideae*. The body of the hyoid bone is developed dorsal to the tract of the thyro-glossal duct, but may invade it (Fig. 320). Remnants of the duct or of secondary detached acini of the thyroid may persist and form cysts or thyroid tumours in the base of the tongue above the hyoid, and commonly

have the power of compelling the mesoderm it invades to become lymphoid in nature [13].

The thymus reaches its fullest growth in early childhood (3rd or 4th year), and continues large as long as the body is in a state of active growth. It begins to shrivel up when maturity is reached, and only a remnant is left as a rule, less remaining in men than in women [14]. It receives its blood supply from the 4th aortic arches through the internal mammary. In manner of origin it resembles the tonsil; indeed, it may be regarded as a buried tonsil. There is a profuse production of lymphoid cells in the gill clefts of fishes, many of which wander out, and by their phagocytic properties help to keep the gill surfaces clean. This fact throws some light on the origin of so much lymphoid tissue from the 2nd and 3rd cleft recesses in higher animals.

The Thyroid [15].—The site at which the thyroid gland arises is shown in Fig. 296, p. 346—on the floor of the pharynx behind the tuberculum impar and exactly in the middle line. The endoderm of the retro-mandibular groove gives rise to a saccular diverticulum almost as soon as the fore-gut becomes differentiated—early in the 4th week of development. Indeed, it is the first of all glandular structures to be differentiated. Immediately in front of the thyroid evagination arises the buccal part of the tongue; behind it is produced the pharyngeal part. The foramen cecum in the sulcus terminalis marks the site at which the thyroid evagination began (Fig. 310, *B*). The endodermal vesicle thus formed grows downwards and backwards through the tissue in which the body of the hyoid will be formed, and as it extends, bifurcates. The stalk of the evagination, at first hollow, apparently represents a duct. The stalk quickly becomes solid, breaks up and by the 6th week has disappeared. The epithelium of the main body of the outgrowth proliferates, and in the 7th week forms a transverse plate ventral to the larynx (Fig. 297). The plate is invaded and broken up into reticulating columns by the surrounding mesoderm. In the 3rd month the epithelial cells become arranged as follicles; these at a later date are converted into vesicles. The original plate assumes a bent or horse-shoe form, the middle part forming the isthmus, the side parts the lateral lobes (Figs. 318, 319).

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Para-thyroids.—There are usually two para-thyroid or *epithelial* hodies on each side, an upper and a lower (Figs. 318, 319). Both are usually applied to the deep or posterior aspect of the thyroid body, the upper being situated amongst the terminal branches of the superior thyroid artery, the lower amongst the branches of the inferior [21]. They are flattened hodies, about 6 to 8 mm. in diameter, yellowish in colour when contrasted with the substance of the thyroid, but they cannot be recognized with certainty, except by their microscopic structure. Their origin is shown in Fig. 317: the lower hodies (*III*) arise from the dorsal recess of the 3rd pair of pouches; they are drawn into a low position by their attachment to the stalk of the thymus (see Figs. 318, 319). The upper para-thyroids (*IV*) arise from the 4th pair of pouches, and become more or less united to the lateral thyroid buds (Fig. 319). In structure they are made up of reticulating columns of cells, with vessels arranged between the columns. It has been proved that their secretion regulates the calcium content of the blood. They have therefore the most intimate concern with the deposition and absorption of bone. How such hodies came to have their origin in the pharynx is still obscure. Parathyroid tissue may be drawn into the superior mediastinum by the thymus and there give rise to tumours [22].

Retropharyngeal Diverticula.—Diverticula occur in the hinder wall and also on the lateral wall of the pharynx, on a level with the cricoid cartilage. Such diverticula are not of developmental origin but are acquired herniations [23]. Nevertheless, developmental diverticula do occur in a retro-cricoid position in some animals [24].

NOTES AND REFERENCES

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[3] Hellman, T. J., *Upsala laekaref. Föerhande.*, 1921, 26, 1; Arey and Others, *Anat. Rec.*, 1935, 64, 9 (taste papillae reach their maximum number in the 3rd decade); Hou-Jensen, H. M., *Zeitsch. Anat. Entwickl.*, 1934, 102, 348 (taste buds in papillae foliatae).

[4] Wood-Jones, F., *Jour. Anat.*, 1918, 52, 345.

[5] Negus, V., *The Mechanism of the Larynx*, 1929; Schaffer, J., *Anat. Hefte*, 1907, 33, 455.

[6] Rubashkin, W., *Anat. Hefte*, 1912, 46, 343.

[7] Just behind the main parotid bud there is a minor epithelial outgrowth that becomes separated from its point of origin and takes up a position in the wall of the pharynx, just internal to the ascending ramus of the mandible. In the 3rd month it is invaded by lymphoid cells and disappears. It was first described

between the genio-glossus muscles [18]. They may also occur between the hyoid and thyro-hyoid membrane. The supra-hyoid or infra-hyoid bursae may also become cystic, and may be mistaken for thyro-glossal cysts (see Fig. 320).

In lower vertebrates the lateral lobes of the thyroid are situated under the mandible. It is not uncommon to find in the right submaxillary region of man a thyroid tumour or cyst, evidently arising from an arrest in the descent of a part or of the whole of a lateral lobe. Aberrant masses of thyroid are often met with in the neck, and frequently become the site of cystic tumours. Occasionally the lumen may persist in the

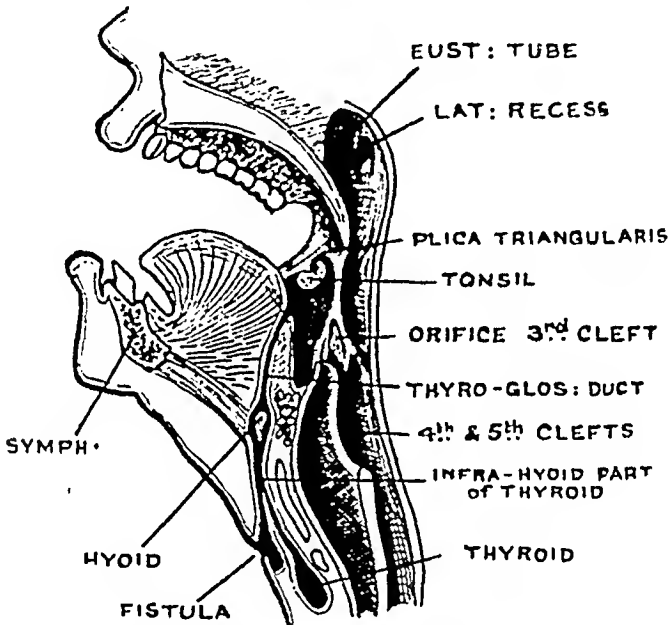


FIG. 320. Section of the Pharynx to show the Track of the developing Thyroid. In rare cases there is a fistula connected with the thyroid, which opens in front of the larynx. The point of origin of the thymus outgrowth from the 3rd cleft may be marked by a recess containing lymphoid tissue as is represented in the figure. The pyriform fossa occurs at the site of the 4th and 5th clefts. The group of mucous glands in front of the epiglottis may give rise to cystic tumours.

median thyroid and open as a fistula in front of the larynx (Fig. 320). Thyroid tissue has been observed in tumours of the ovary [19].

Ultimate Branchial Bodies.—In Fig. 317, *B*, is represented the endodermal outgrowth from the 5th or ultimate pharyngeal pouch. Like the thymic buds the lateral thyroid buds and superior parathyroids (*IV*) lose their connection with the embryonic pharynx early in the 7th week. The pyriform fossa, within the ala of the thyroid cartilage marks their point of origin (Fig. 320). The blood supply suggests the double origin of the thyroid gland, for while the superior arteries supply the area assigned to the median outgrowth, the dorsal parts of the lateral lobes are nourished by the inferior thyroid branches of the 4th aortic arch [20]. The superior vessels represent the original arterial supply.

Para-thyroids.—There are usually two para-thyroid or *epithelial* bodies on each side, an upper and a lower (Figs. 318, 319). Both are usually applied to the deep or posterior aspect of the thyroid body, the upper being situated amongst the terminal branches of the superior thyroid artery, the lower amongst the branches of the inferior [21]. They are flattened bodies, about 6 to 8 mm. in diameter, yellowish in colour when contrasted with the substance of the thyroid, but they cannot be recognized with certainty except by their microscopic structure. Their origin is shown in Fig. 317: the lower bodies (*III*) arise from the dorsal recess of the 3rd pair of pouches; they are drawn into a low position by their attachment to the stalk of the thymus (see Figs. 318, 319). The upper para-thyroids (*IV*) arise from the 4th pair of pouches, and become more or less united to the lateral thyroid buds (Fig. 319). In structure they are made up of reticulating columns of cells, with vessels arranged between the columns. It has been proved that their secretion regulates the calcium content of the blood. They have therefore the most intimate concern with the deposition and absorption of bone. How such bodies came to have their origin in the pharynx is still obscure. Parathyroid tissue may be drawn into the superior mediastinum by the thymus and there give rise to tumours [22].

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[23] Keith, Sir A., see note [18].

[24] Negus, V., *Monatsch. Ohrenheilk. Laryng.*, 1931, 65, 1388.

CHAPTER XX

ORGANS OF DIGESTION

Divisions of the Alimentary Tract.—It is advantageous to approach the development of every system of the body by a recapitulation of the various evolutionary stages, so far as these stages are known to us. As regards the evolution of the various parts of the alimentary system, comparative anatomy does not help us greatly, because in even the lowest forms of vertebrates the main parts are already present—the mouth,

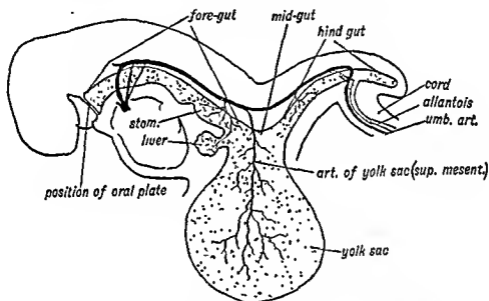


FIG. 321. The Form of the Alimentary Canal in a Human Embryo at the end of the 4th week.

oesophagus, stomach, liver and intestine. In tracing the development of the earliest digestive cavity (archenteron) of the human embryo (p. 57) we saw that its origin was essentially similar to that of the lower invertebrates and that the original mouth apparently became converted into blastopore, primitive streak and cloacal membrane. A new mouth is formed by the breaking down of the buccopharyngeal membrane (oral plate, Fig. 321) early in the 4th week; we shall see that a new kind of vent or anus is formed at a later stage in the development of the human embryo—namely, at the end of the 2nd month of development. There are other reasons why comparative anatomy does not help us to understand the early stages in the development of the alimentary system,

1855) by a Danish anatomist, Dr. Chievitz, and hence is known as the organ of Chievitz. Its significance is not known. See Broman's *Entwicklung des Menschen*, 1927; Ramsay, A. J., *Anat. Rec.*, 1935, 63, 281. In the parotid and submaxillary glands lymphoid nodules are often formed at the end of the 3rd month (Bairati, A., *Archiv. Biol.*, 1932, 43, 415).

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wall, and an inner to the endoderm or archenteron to form the visceral wall or splanchnopleure [2]. The cavity formed by the cleavage of the mesoderm is the coelom (Fig. 49). Originally the cavity was designed for the purposes of excretion; its wall also served as a nidus for the reproductive cells. In vertebrates the coelom came to serve the purposes of a large bursa, in order that the muscular movements of the digestive canal, lungs and heart might proceed without undue friction. Hence the alimentary canal is developed within the cavity of the coelom, being enclosed by the median partition or mesentery, which separates the right

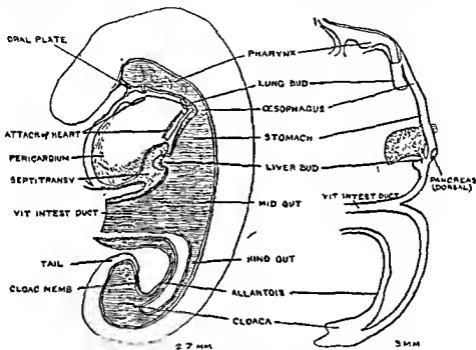


FIG. 322.

FIG. 323.

FIG. 322. The Alimentary System of a Human Embryo 2.5 mm. long, and near the end of the 4th week of development. (Prof. Peter Thompson.)

FIG. 323. The Alimentary System of a Human Embryo, although only 3 mm. long, is in the stage of development reached at the end of the 5th week. (After Prof. Broman.)

coelomic space from the left. The median partition, by which the alimentary canal is suspended from the dorsal or vertebral wall of the body cavity, forms the *primitive dorsal mesentery*; the part of the median partition that fixes the tract to the anterior or ventral wall of the body cavity is known as the *primitive ventral mesentery*, which, however, is formed only in connection with the fore-gut and the cloacal segment of the hind-gut, all the rest being destitute of a ventral mesentery from the beginning. Hence the right and left coelomic spaces in the abdomen are thrown into one, and form the peritoneal cavity. The only parts of the alimentary canal that never come to lie within the coelom are the anterior

which will be explained by a reference to Fig. 321. In the human embryo a part of the alimentary canal has become specialized and precociously developed to form the yolk sac, a provision for the nourishment of the embryo ; these embryonic adaptations mask and obliterate the ancestral stages in the evolution of the bowel (see p. 16).

With the development of the cephalic and caudal extensions of the embryonic plate the archenteron becomes differentiated into three parts (Fig. 322)—the *Mid-gut*, which represents the central and chief part of the primitive cavity ; the *Fore-gut* and *Hind-gut* [1]. There can be no doubt these represent three functional divisions. The mid-gut is supplied by the superior mesenteric artery and serves for one kind of digestion and absorption ; the hind-gut, supplied by the inferior mesenteric artery, is mainly excretory in nature ; the fore-gut, separated by the outgrowth of the liver from the mid-gut, is supplied mainly by the coeliac axis and serves the preparatory purposes of digestion. The pharynx, respiratory tract, oesophagus, stomach, liver and pancreas represent parts of the fore-gut. The hind-gut begins on the proximal side of the splenic flexure and extends to the anus ; the allantois, bladder and urethra are separated from its hinder end—the cloaca.

Differentiation of Parts.—How rapidly the various parts of the alimentary system are differentiated during the 5th week of development will be seen by comparing Figs. 322 and 323. Fig. 322, which represents the alimentary tract of a human embryo near the end of the 4th week, shows the pharynx of large size, the lung bud beginning to evaginate from the floor of the fore-gut just behind the pharynx and at this date lying directly under the occipital part of the head ; the oesophagus and stomach and first part of the duodenum scarcely marked off from one another, all of them lying on the dorsal wall of the pericardium and directly under the cervical segments of the embryo. The evagination to form the liver indicates the junction of the fore-gut with the mid-gut. The latter division is in wide communication with the yolk sac. The various parts of the hind-gut are already indicated. The condition towards the end of the 5th week is shown in Fig. 323. The oral membrane is gone ; the pharynx is relatively smaller ; the outgrowth of the pulmonary system is now very apparent, the oesophagus and stomach are longer and narrower ; the liver outgrowth has become massive ; the mid-gut is tubular and V-shaped while the neck of the yolk is reduced to a duct (vitello-intestinal duct). The parts of the hind-gut have assumed a more definite shape.

Primitive Mesentery and Coelom.—It will be remembered that almost as soon as it appears, the ventral mesoderm becomes cleft into two layers—an outer applied to the ectoderm to form the somatopleure or body-

astinum, some distance above the diaphragm [5]. This congenital condition must not be confused with herniation of part of the stomach and peritoneum through the oesophageal opening in the diaphragm, an acquisition of adult life.

Development of the Liver [6].—Before proceeding to describe the development of the stomach, it is convenient to deal first with the liver, because the manner in which this viscus arises gives the key to the

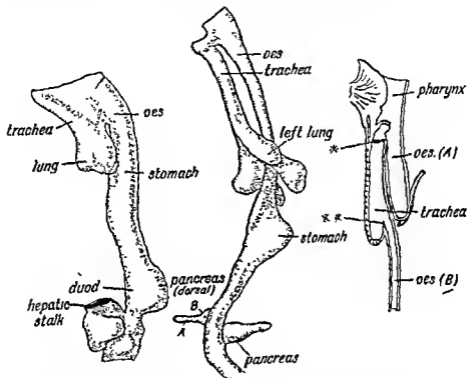


FIG. 324.

FIG. 325

FIG. 326.

FIG. 324 Fore-gut of an Embryo in the 4th week of development. (Broman.)

FIG. 325 Fore-gut of an Embryo at the end of the 5th week of development. A, gall-bladder; B, hepatic stalk which gives off ventral bud of pancreas (Broman.)

FIG. 326 Irregular Separation of the Trachea and Oesophagus. The upper or pharyngeal part of the oesophagus forms a blind sac; the lower part passes from the trachea to the stomach. *, Upper end of "abnormal" septum between oesophagus and trachea; **, upper end of the "normal" septum.

complicated developmental changes of the abdominal viscera. The human liver in its development repeats broadly the forms met with in ascending the animal scale. In amphioxus the liver is merely a caecal diverticulum of the digestive canal; in amphibians it is a modified tubular gland—the hepatic cells being arranged in cylinders around the bile ducts. In mammals the tubular arrangement is lost and a lobular form substituted. In every case it is so placed that the blood, laden with the products of absorption from the alimentary tract or from the placenta, must come into intimate relationship with the hepatic tissue

part or pharynx and the most posterior part of the cloaca. The anterior part of the coelomic space becomes the cavity of the pericardium; it lies beneath the pharynx (Fig. 322) and is separated from the peritoneal space by a transverse partition, the *septum transversum* [3], already well marked at the beginning of the 4th week. The primitive oesophagus crosses the upper or dorsal border of the septum transversum (Fig. 327). At each side of it is situated a communication between the pericardial and peritoneal spaces—the *pleuro-peritoneal passages*. These two passages are separated not only by the primitive oesophagus but also by the primitive median mesentery, which encloses the oesophagus (Fig. 327).

Oesophagus.—In the 4th week the oesophagus of the human embryo resembles that of a fish; it is merely a sphincter or constricted part between the pharynx and stomach (Fig. 322). During the 6th and 7th weeks, when the neck is being differentiated and the pharynx and head separated from the heart and thorax, the oesophagus undergoes a rapid elongation. The chief cause of the elongation of the oesophagus is to be sought for in the development of the lungs and pleural cavities (Fig. 325), by which the stomach is forced backwards in the body cavity. The oesophagus is of double origin; the upper or retrotracheal part is derived with the trachea from the pharyngeal segment of the fore-gut; the lower or infratracheal part arises from the pregastric segment of the fore-gut. In the 5th week the pulmonary bud and tracheal groove are being separated from the oesophagus, the lateral septa that effect the separation beginning behind and spreading forwards (Figs. 324, 325). Children are sometimes born in which the process of separation has taken place in an irregular manner (Fig. 326). The retrotracheal part ends blindly, and is surrounded by striated pharyngeal musculature; the infratracheal part opens from the trachea, and is covered by non-striated muscle [4]. The oesophagus is at first lined by columnar epithelium, but in the 2nd month as it elongates the epithelium proliferates, forming several irregular layers, which almost occlude the lumen of the tube for a time. In the 5th month glands are formed in the submucous tissue. In the 6th week the oesophagus is only 2 mm. long; at birth it measures 100 mm. (4 in.). Its commencement is surrounded by a sphincter formed by part of the inferior constrictor of the pharynx; above this sphincter, in later life, a pouch (*retropharyngeal diverticulum*) may arise; such pouches are never congenital in origin (see p. 377). At the lower or distal end the oesophagus is also closed by a sphincter. The muscle coats are differentiated in the 7th week, the circular first, the longitudinal later. The stomach may be arrested in its backward migration, so that the cardia lies in the posterior medi-

right and left masses do not correspond to the right and left lobes of the fully formed liver; the separation between the right and left lobes is formed late, and has no functional significance. A line from the fundus of the gall bladder to the caval impression divides the liver into embryonic and functional right and left halves (Cantlie).

The hepatic buds are developed just behind the sinus venosus and between the vitelline veins, which are also situated in the ventral mesentery (Figs. 327, 329), but the main stems of the umbilical veins

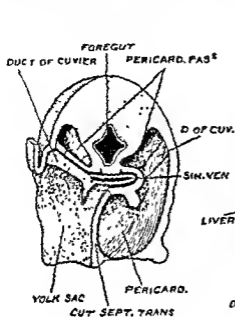


FIG. 328

FIG. 328. Dissection of the Septum Transversum of a Human Embryo, viewed on its cephalic aspect, early in the 4th week of development. The left half is cut away to expose the yolk sac. (After Low)

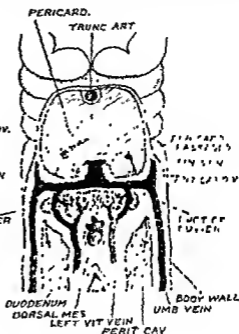


FIG. 329

FIG. 329. Coronal section of the Septum Transversum of a Human Embryo in the 5th week of development, showing the liver trabeculae invading, and being invaded by, the terminal parts of the vitelline veins. (After Hix)

lying in the body wall (Fig. 329) are not involved and come to lie on each side of the developing liver (Figs. 330, 331). The veins are broken up by the ingrowth; from them starts an invasion of sinus-like capillaries which, with the surrounding mesoderm, penetrates the liver bud and breaks the solid endodermal processes into reticulating cylinders. According to F. T. Lewis the hepatic processes perforate and proliferate within the lumina of the vitelline veins, the venous capillaries thus arising directly from venous spaces. Secondary processes arise from the primary hepatic reticulating cylinders and form smaller and smaller meshes of hepatic cells. The hepatic cells, first grouped in trabeculae, become arranged in lobular units; round the periphery of the units

right and left masses do not correspond to the right and left lobes of the fully formed liver; the separation between the right and left lobes is formed late, and has no functional significance. A line from the fundus of the gall bladder to the caval impression divides the liver into embryonic and functional right and left halves (Cantlie).

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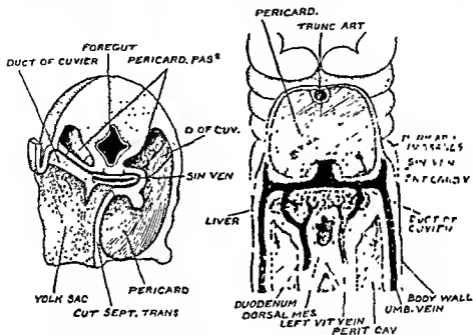


FIG 328

FIG 329

FIG 328 Dissection of the Septum Transversum of a Human Embryo, viewed on its cephalic aspect, early in the 4th week of development. The left half is cut away to expose the yolk sac. (After Low.)

FIG 329 Coronal section of the Septum Transversum of a Human Embryo in the 5th week of development, showing the liver trabeculae invading, and being invaded by, the terminal parts of the vitelline veins (After Ellis)

lying in the body wall (Fig. 329) are not involved and come to lie on each side of the developing liver (Figs. 330, 331). The veins are broken up by the ingrowth; from them starts an invasion of sinus-like capillaries which, with the surrounding mesoderm, penetrates the liver bud and breaks the solid endodermal processes into reticulating cylinders. According to F. T. Lewis the hepatic processes perforate and proliferate within the lumina of the vitelline veins, the venous capillaries thus arising directly from venous spaces. Secondary processes arise from the primary hepatic reticulating cylinders and form smaller and smaller meshes of hepatic cells. The hepatic cells, first grouped in trabeculae, become arranged in lobular units; round the periphery of the units

are the terminal portal venules ; in the centre of each unit is the beginning of a tributary to the hepatic vein ; the portal or placental blood as it passes from the periphery to the centre of each lobule is exposed to the action of the liver cells. Growth takes place by successive division or dichotomy of the lobules ; the chief areas of proliferation save sub-capsular, being always at the surface of the organ. Growth is particularly rapid during the 2nd and 3rd months, the liver reaching its largest relative size at this time. At birth there are over half a million lobules. Up to the 10th week, when the foetus is 42 mm. long, the right and left halves have grown symmetrically, but then occur the retraction of the bowel from the umbilical cord and the enlargement of the stomach, leading to an atrophy of part of the left lobe. The *ducts within the liver*, unlike those

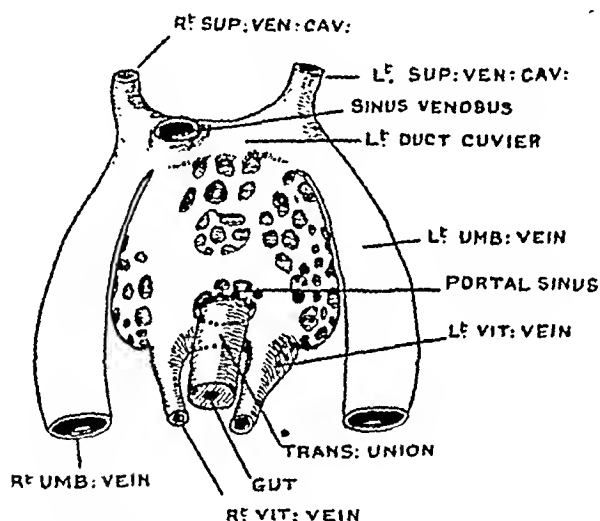


FIG. 330. The Liver Mass Invading the Vitelline Veins early in the 5th week. (Mall.)

of any other gland, arise by a secondary process. Undifferentiated tissue lying along the distribution of the portal vein in the liver, group themselves into cords, develop lumina, become covered by mesodermal tissue and thus form the intra-hepatic bile ducts.

Veins of the Liver.—Within the liver the two vitelline veins become divided so as to form two sets of vessels—afferent or distributing and efferent or collecting veins. In the 6th week a number of remarkable changes occur : (i) the left umbilical vein, which opens at first in the left duct of Cuvier (Fig. 329), establishes a communication with the portal sinus in the transverse fissure of the liver (Fig. 331) ; (ii) the right umbilical vein disappears ; (iii) a new channel—the *ductus venosus*—is opened between the portal sinus and the inferior vena cava ; (iv) a subdiaphragmatic communication opens up between the terminal parts of the vitelline veins, to become the left hepatic stem (Fig. 331) ; (v) the

right vitelline vein, all except its terminal part, becomes obliterated (Fig. 331).

Gall Bladder and Bile Ducts.—The hepatic diverticulum, from which the liver buds arise, may be regarded as a direct extension of the fore-gut. From its hinder part (Fig. 324) are developed the common bile duct, the gall bladder, and the cystic duct which is formed at the junction of the gall bladder and common bile duct. The hepatic ducts arise within the solid liver outgrowths. At first the gall bladder lies in the ventral mesentery (gastro-hepatic omentum or ligament)—a position that is permanent in some vertebrates and may occur as an anomaly in man. In the 2nd month it becomes embedded in the hepatic tissue, its fundus

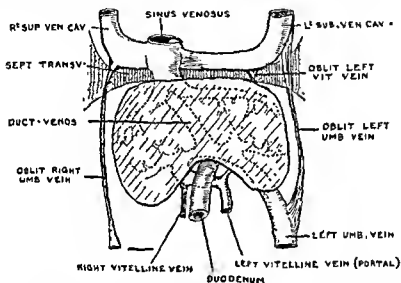


FIG. 331. Diagram to show the Transformation in the Veins to the Liver at the end of the 6th week. (After Mall)

appearing on the diaphragmatic surface; at a later date it assumes its superficial position. The lumen of the gall bladder and also of the ducts is occluded by an epithelial proliferation during the 2nd month, as also is the lumen of the duodenum. Shallow diverticuli are formed in the wall of the main ducts. Children are sometimes born with atresia of the gall bladder and of the hepatic duct system [7]. The coats of the gall bladder become differentiated in the 3rd month, the muscular coat corresponding to the muscularis mucosa of the intestine. A spiral ridge becomes developed in the neck of the bladder in the 4th month, glands appearing in the mucous membrane of the neck about the same time [8]. Originally its veins end in the adjoining hepatic tissue. Occasionally the bud for the gall bladder divides, giving rise to a bifid or double gall bladder. Round the termination of the common bile duct, which is devoid of a muscular coat, a sphincter is developed from the

musculature of the duodenum (see p. 400). The manner in which the common bile duct, hepatic artery and portal vein come to occupy the free edge of the ventral mesogastrium will be described in another paragraph. In some animals, such as the rat and horse, the gall bladder is absent [9]. The gall bladder is for the concentration of bile; it is absent in animals (herbivora) in which the bile is plentiful and dilute (Schmidt and Ivy). Bile begins to be excreted by the liver in the 12th week [10].

Separation of the Liver from the Septum Transversum.—As the liver develops, the dorsal and ventral mesenteries of the fore-gut, in the sub-

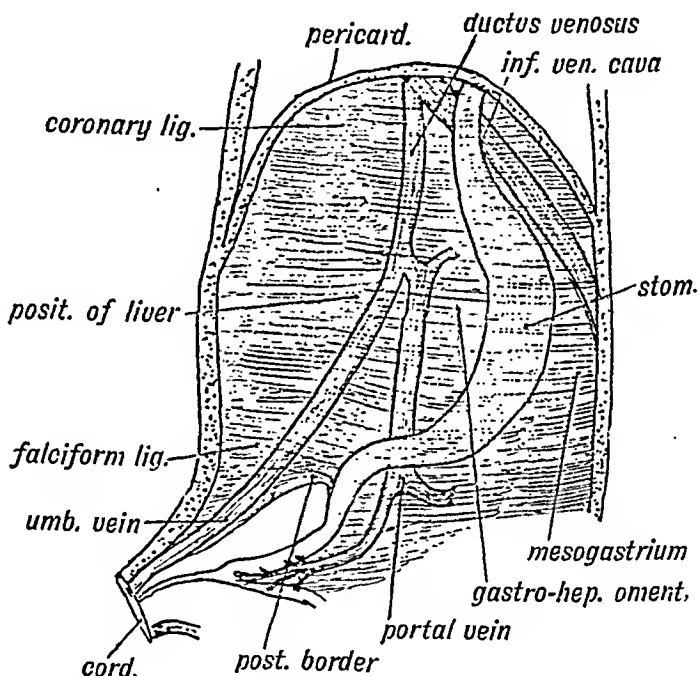


FIG. 332. The origin of the Peritoneal Ligaments which connect the Liver with surrounding parts from the primitive mesenteric sheet. The liver is supposed to have been removed, leaving the primitive mesentery intact.

stance of which the liver and stomach are formed, become differentiated from the tissues of the septum transversum. The typical arrangement of these membranes, as seen in reptiles, is shown in Fig. 332. In the dorsal mesentery (mesogastrium) lie the inferior vena cava and arteries of the fore-gut; in the ventral mesentery (gastro-hepatic omentum) are contained the terminal parts of three veins—the umbilical, portal and inferior vena cava, the last vessel reaching the ventral mesentery by passing to the right of the oesophagus. The liver develops within both ventral and dorsal mesenteries, but that part of the mesentery in which it and the inferior vena cava lie—the *mesohepar*—becomes separated from the part that is occupied by the bile ducts, portal vein and the

stomach (Fig. 333). Broman found that this separation, which occurs in all higher vertebrates, takes place towards the end of the 4th week in the human embryo, by the development of a recess in the mesentery—the *mesenteric recess*—which commences on the right side of the duodenum and extends forwards (see Fig. 335). The mesenteric recess [11] (*bursa omentalis*, Broman) forms the vestibular or hepatic part of the lesser sac of the peritoneum, and extends from the foramen of Winslow to behind the Spigelian lobe of the liver (see Figs. 334, 335 and 336). When the liver and stomach are removed in the course of dissection, the attachment of the mesohepar (mesohepaticum, Fig. 336) will be seen to bound the Spigelian part of the lesser sac on the right, while on its left side, the dorsal mesogastrium has been evaginated to form the main

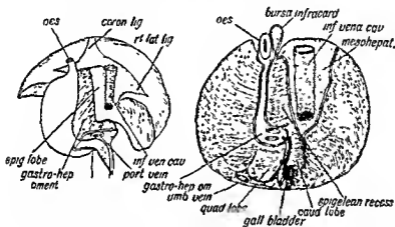


FIG. 333.

FIG. 334.

FIG. 333 The Liver viewed from behind to show its relationship to the gastro-hepatic omentum, part of the ventral mesentery

FIG. 334 The Visceral Surface of the Liver of a Foetus, 16 mm. in the 7th week of development. (P. Thompson)

body of the lesser sac. Thus it will be seen that the dorsal and ventral mesenteries of the fore-gut are split into a right lamina (the *mesohepar*) and a left lamina (the *mesogastrium*) by the development of a recess that forms the earliest and first part of the *lesser sac*. The mesenteric recess at first extends forwards in the mesentery of the oesophagus almost to the right lung bud—a condition that is constant in reptiles. There is a corresponding forward prolongation on the left side of the oesophagus. When the lungs expand and the diaphragm is being formed during the 7th week, the apical part of the mesenteric recess is cut off and left within the thorax—to the right of the oesophagus and just above the diaphragm. To this detached part Broman has given the name of *infra-cardiac bursa* (Fig. 334). It usually disappears at the end of foetal life, but a remnant can often be found in the posterior

mediastinum of adults if careful search is made. The peritoneal prolongation on the left side disappears at the same time.

Ligaments of the Liver.—When the liver separates from the septum transversum towards the end of the 2nd month of development, it is attached to the walls of the abdomen by peritoneal ligaments derived from the dorsal and ventral mesenteries of the fore-gut (Figs. 332, 333). These are the following :

1. The *gastro-hepatic omentum*, or ligament, is that part of the ventral mesentery which passes from (i) the oesophagus, (ii) lesser curvature

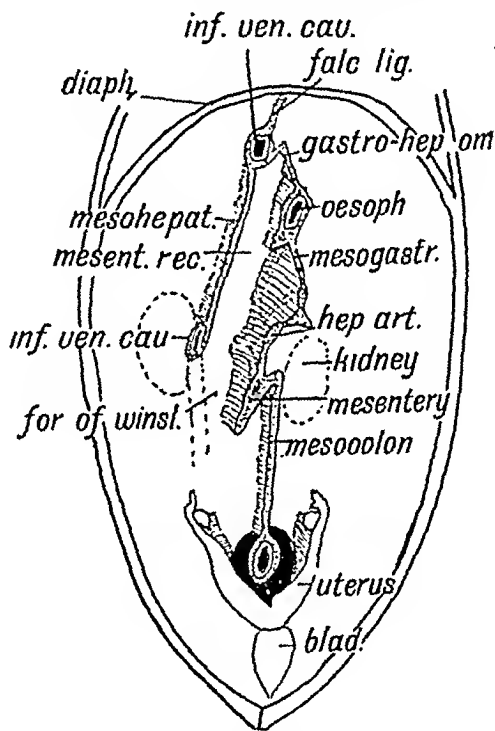


FIG. 335. Diagram of the Primitive Attachments of the Visceral Mesenteries to the Posterior Wall of the Abdomen as seen in a Low Primate (*Lemur coronatus*). The condition illustrates an early developmental phase in the human foetus.

or ventral border of stomach, and (iii) first stage of duodenum to (i) the diaphragm, (ii) the posterior part of the longitudinal fissure of the liver, the ductus venosus lying within its hepatic attachment, and (iii) the transverse fissure of the liver (Fig. 333). The portal and umbilical veins lie in the ventral mesentery (Fig. 332); the hepatic artery passes by it to the liver. The right or free border of the gastro-hepatic omentum, with the falciform ligament containing the remnant of the umbilical vein, represents the posterior border of the primitive ventral mesentery (Fig. 332).

2. The *falciform ligament*, containing the umbilical vein, also represents part of the ventral mesentery. At an early stage of development (Fig. 329) the umbilical veins reach the sinus venosus by passing through

the septum transversum. The terminal parts of both veins become obliterated (Fig. 331); the new terminal channel for the left vein is formed in the ventral mesentery.

3. *Coronary, right and left lateral ligaments; attachments to vena cava and to diaphragm.*—These ligaments, which are the strongest hepatic bonds, are derived from the mesohepar in the latter part of the 2nd month, when the liver is being separated from the diaphragm by invading pockets or recesses of peritoneum. It would be convenient to retain the term *mesohepar* as a name for all adult bonds that bind the

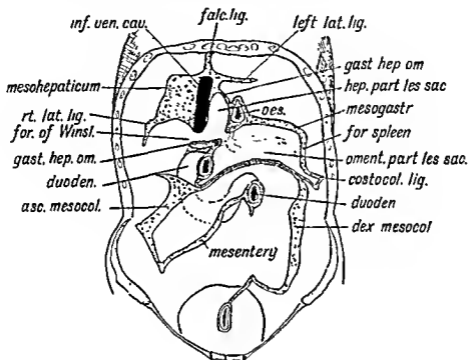


FIG 331

liver to the diaphragm, looking on the right and left lateral ligaments as mere processes of the mesohepar.

Morphology of the Liver [12].—The liver in upright or orthograde primates—a group to which man and anthropoid apes belong—differs widely in form and lobulation from that of mammals generally, but traces of the fissures and lobes of the typical mammalian liver can often be found in the human organ. The liver of a dog or of a dog-like ape consists of three main lobes—right, middle and left—and two accessory lobes, the *spigelian* and *caudate* (Fig. 337). In man, the right and middle lobes are united, but traces of the fissure that should separate them (the right lateral) are frequently to be seen in the liver of the newly born

child (Fig. 338). The caudate lobe has become reduced in man to a vestige, but in the 3rd-month foetus it is of considerable size (Figs. 334, 338). It projects from the liver at the upper boundary of the foramen of Winslow; in many animals it rivals the right lobe in size. The

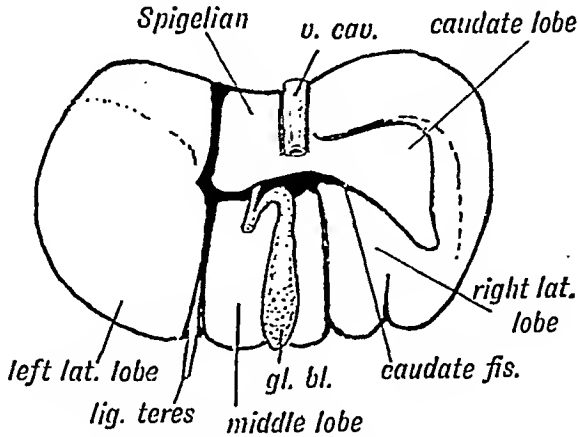


FIG. 337. Diagram of a Mammalian Liver viewed on its ventral aspect.

caudate fissure separates the caudate from the right lobe, and a trace of this fissure is very frequently to be observed in the human liver (Fig. 338). Irregular lobulation of the liver is not uncommon; the condition seen in the 6th week, when the gall bladder and umbilical vein occupy

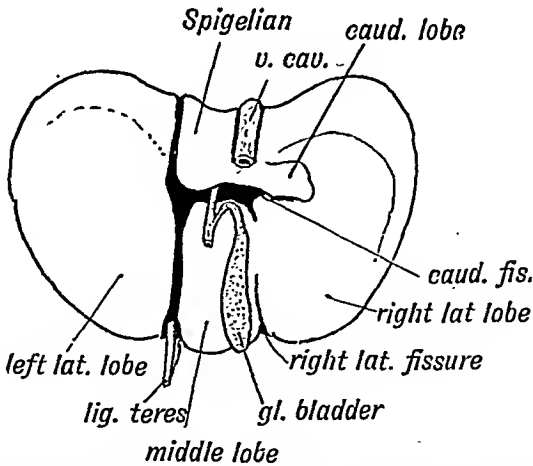


FIG. 338. The lower surface of the Liver of a Human Foetus during the 3rd month, showing vestiges of fissures and lobes of the typical mammalian Liver.

a common fissure, may be retained. The quadrate lobe arises in the 7th week from the left lobe (Fig. 334) and grows across the fissure occupied by the umbilical vein to occupy the space between the vein and gall bladder (P. Thompson). The structures in the transverse fissure, especially the hepatic artery, show a wide range of individual variation [13].

Changes in the Liver after Birth.—During foetal life the liver increases rapidly in volume in comparison with the other abdominal organs, attaining its largest size relative to other organs in the 3rd month (Frazer). At birth it occupies nearly half of the abdominal space, and measures one-thirteenth of its final volume. The left lobe may still reach, and even overlap, the spleen. Up to the time of birth nucleated red blood corpuscles multiply within it (p. 468). After birth two factors come into operation that lead to a diminution in size and change of shape. It is supplied before birth by placental instead of portal blood; at birth, its blood-forming function ceases; its rate of growth becomes proportionately less than that of other abdominal organs. The stomach, formerly empty, becomes now filled, and presses the liver towards the right side, causing a change in shape and partial atrophy of the left lobe. Riedel's lobe is a linguiform prolongation of the right lobe below the 10th right costal cartilage caused by compression of the waist. It is never present at birth.

The Stomach.—The stomach is developed out of that part of the fore-gut which lies between the oesophagus and pharynx in front and the yolk sac, duodenum and liver bud behind. In the 4th week (Fig. 322) the stomach is situated in the neck, with the cervical somites dorsal to it, the pericardium ventral to it, while on each side is the coelomic passage, which leads from the pericardial to the peritoneal spaces (Fig. 327). At this time heart, lungs and stomach lie near the exit of the vagal fibres from the central nervous system. During the 6th and 7th weeks, as we have already seen, the growth of the lung buds leads to an elongation of the oesophagus and a backward migration of the stomach, which, from being a cervical structure, comes to lie level with the lower thoracic segments. At first its dorsal and ventral mesenteries are undifferentiated from the septum transversum. In the 5th week the gastric part of the fore-gut shows a dorsal bulging—the greater curvature (Fig. 325). As the liver and gut are developed, the stomach separates itself from the septum transversum and comes to be suspended from the dorsal wall of the coelom by the *dorsal mesogastrium* (Fig. 332). The gastro-hepatic omentum is part of the *ventral mesogastrium*. The oesophageal end of the stomach lies between the vertebral or spinal fibres of the diaphragm, which develop in its mesentery; the outgrowth of the liver bud fixes its pyloric end in the ventral mesogastrium. Three changes quickly ensue during the 6th and 7th weeks, the one being partly dependent on the other:

(i) The dorsal border of the stomach, to which the dorsal mesogastrium is attached, grows more rapidly than the ventral border to which the ventral mesogastrium is attached. The *greater and lesser curvatures* are thus produced.

(ii) The *fundus* of the stomach is produced as an outgrowth from the dorsal border, its origin being similar to that of the caecum from the large intestine (Fig. 339, A).

(iii) While a ventral mesogastrium attached to the lesser curvature undergoes a relatively slow growth, the dorsal mesogastrium is affected by a very rapid expansion (Figs. 341, 342). Because of the discrepancy in the growth of these two membranes, the greater curvature of the stomach becomes freely movable, while the lesser curvature remains relatively fixed.

The three factors just enumerated lead to a rotation of the stomach, the greater curvature moving to the left, while the surfaces formerly

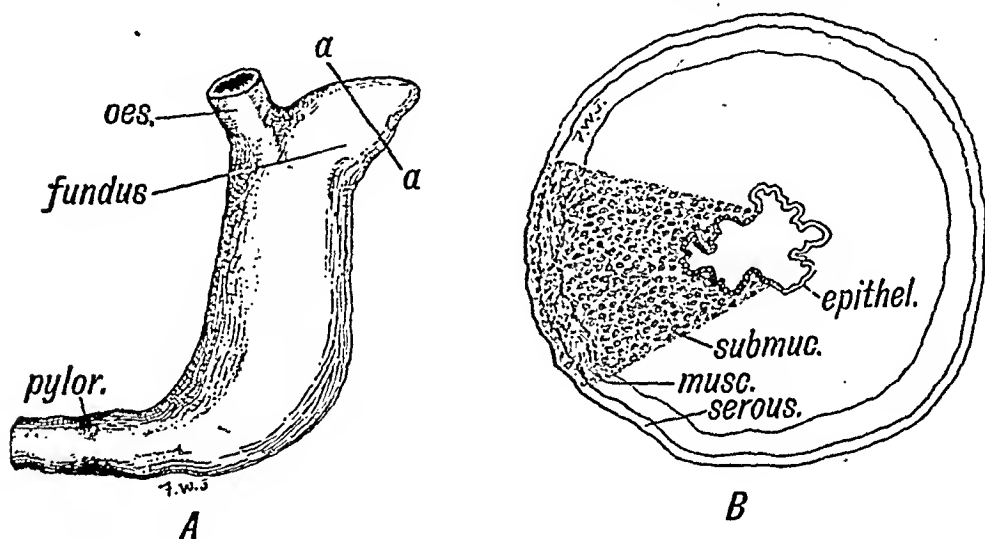


FIG. 339.

- A. Stomach of a Human Foetus about the end of the 3rd month, showing the outgrowth of the Fundus of the Stomach. (Wood-Jones.)
 B. Section across the Fundus (the line of section is indicated in A), showing the differentiation of the four coats of the stomach. (Wood-Jones.)

right and left, carrying the corresponding vagus nerves, become posterior and anterior. Rotation is already evident in the 5th week of development (Broman). All of these changes are adaptations to allow the stomach to expand when filled and contract when emptied. As the stomach fills, it is the greater curvature that expands; the lesser curvature remains relatively fixed. By the commencement of the 4th month the stomach is demarcated into a wide, vertical, *cardiac* part, and a narrower horizontal or *pyloric* part. The pyloric sphincter becomes differentiated towards the end of the 2nd month, and it is then possible to see a distinction between pylorus and duodenum.

Rotation of the Stomach.—Rotation of the stomach is brought about by a complicated series of growth changes which involve not only the stomach itself but all structures in its neighbourhood. The extent of

these growth changes are made evident in Figs. 341 and 342. In Fig. 341 the stage of rotation early in the 7th week is shown; in Fig. 342, a stage reached in the 8th week. In Fig. 341 the liver has been removed to show the formation of the mesenteric recess and the growth of the omentum along the greater curvature of the stomach. In Fig. 342 the dorsal mesentery of the stomach is shown expanding into the left side of the abdomen, carrying within it the omental extension of the "lesser sac" or mesenteric recess. The exact factor that initiates and brings about the expansion and rotation of the stomach towards the left side

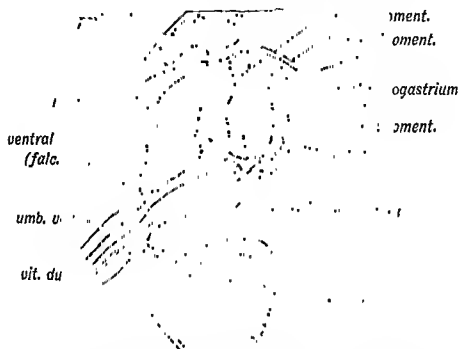


FIG. 340. The Relationship of the Spleen, Pancreas and Liver to the Mesogastrium in the Embryo (purely schematic).

of the body we do not know; the process may be reversed—the pyloric end swinging to the left, the cardiac end to the right. Rotation of the stomach is of ancient origin; it occurs in reptiles [14].

Differentiation of the Coats of the Stomach [15].—A section of the wall of the stomach at the end of the 3rd month of foetal life (Fig. 339, *B*) shows (i) an endodermal lining everywhere thrown into depressions or pits—the *primary gastric pits*—from which gastric glands will be produced during the 4th month; (ii) an extremely thick submucous layer; (iii) a circular muscle coat, with nerve fibres and ganglion cells applied to its outer surface; while the circular coat appears during the 7th week, the outer longitudinal coat is not differentiated until the 4th month; and (iv) peritoneal coat. The primary gastric pits appear at

(ii) The *fundus* of the stomach is produced as an outgrowth from the dorsal border, its origin being similar to that of the caecum from the large intestine (Fig. 339, *A*).

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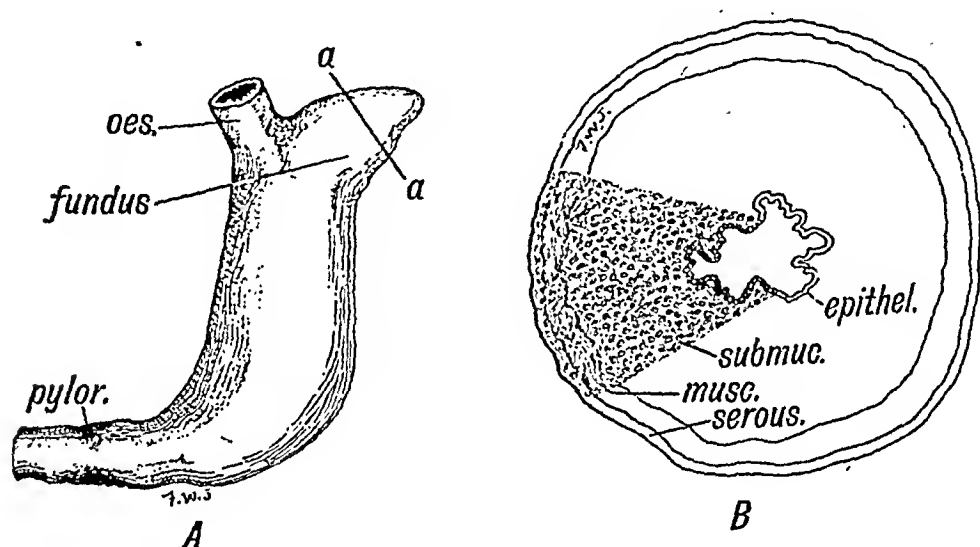


FIG. 339.

A. Stomach of a Human Foetus about the end of the 3rd month, showing the outgrowth of the Fundus of the Stomach. (Wood-Jones.)

B. Section across the Fundus (the line of section is indicated in *A*), showing the differentiation of the four coats of the stomach. (Wood-Jones.)

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Rotation of the Stomach.—Rotation of the stomach is brought about by a complicated series of growth changes which involve not only the stomach itself but all structures in its neighbourhood. The extent of

permeated by fine branches of the splenic artery. This artery is one of the vessels of the mesogastrium (Fig. 313); its branches end in the developing tissues of the spleen and greater curvature of the stomach. The splenic blood spaces are formed during the earlier part of the 3rd month by dilatation of the capillaries, and perhaps also from veins which, in the developing spleen, are lined by columnar cells. The trabecular and muscular tissues, and the capsule, are derived from the mesoderm of the dorsal mesogastrium. Small masses of splenic tissue (accessory spleens) are occasionally formed in the dorsal mesogastrium near the hilum of the spleen. In lower mammals the splenic formation spreads backwards until it forms a colic lobe lying in the dorsal mesentery

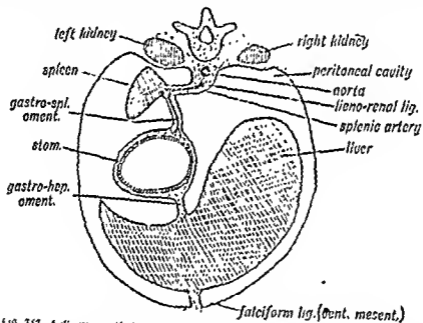


FIG. 313 A diagrammatic transverse section of the Mesogastrium viewed from behind

of the hind-gut [17]. In the 3rd month the surface of the spleen is nodular and deeply incised; about the middle of foetal life the fissures begin to disappear; only on the anterior or gastric border do they persist. The spleen differs from a lymph gland in that its spaces are formed by dilatations of blood capillaries in place of lymph capillaries. The endothelial cells that line the blood spaces and the reticular cells that support the endothelial cells seem to be of the same nature, both adding to the blood a kind of white corpuscle, known as histiocytes. Lymphoid nodules appear in the spleen about the 6th month. Lymphoblasts appear in the blood spaces of the spleen in the 4th month. Presently these give rise to erythroblasts, myeloblasts, megakaryocytes. In the later months of foetal life red corpuscles are formed and so lymphocytes. The development of the spleen in the mesogastrium

the end of the 2nd month ; in the 3rd solid processes grow within the submucous coat, thus forming the epithelial bases of the gastric glands. Parietal cells begin to form at the end of the 3rd month. Even as late as the 5th month of foetal life the mucous membrane in the pyloric region has a villous appearance owing to upgrowths between the mouths of the primary gastric pits. True villi, however, commence at the distal border of the pylorus.

The Spleen [16].—Although the spleen is part of the blood system of the body I have retained it here because its mode of origin shows that it must have been originally a part of the alimentary system. It

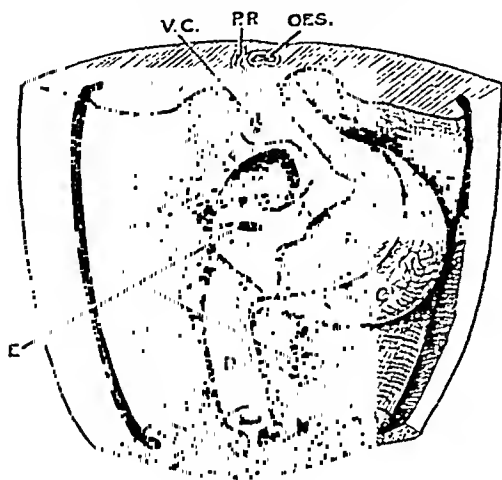


FIG. 341.

FIG. 341. Formation of the Mesenteric Recess and Rotation of the Stomach during the 7th week of development. (After Prof. Frazer.)

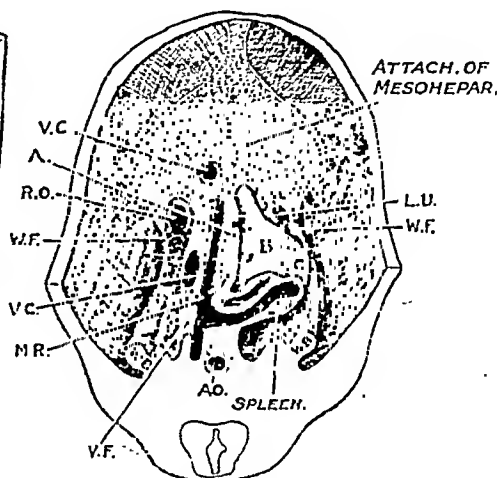


FIG. 342.

FIG. 342. The state of parts in the Subdiaphragmatic Region of the Abdomen, during the 8th week. (After Prentiss.)

A, gastro-hepatic ligament ; B, stomach ; C, great omentum ; D, duodenum ; E, portal vein ; oes., oesophagus ; P.R., pneumatic recess ; V.C., vena cava ; V.F., venous fold of peritoneum ; M.R., mesenteric recess ; W.B., Wolffian body ; A.O., abdominal aorta ; W.F., Wolffian fold ; R.O., right diaphragmatic opening ; L.O., left diaphragmatic opening.

arises in connection with the stomach, and its blood, like that of the alimentary tract, enters the portal circulation. The spleen is formed in the dorsal mesogastrium above the cardiac end of the stomach (Figs. 340, 342) and grows out from the left surface of the mesogastrium (Fig. 343). It appears at the beginning of the 6th week by a localized growth of the mesoderm (mesenchyme) in the mesogastrium. The splenic condensation, as just mentioned, projects on the left aspect of the mesogastrium, the projection being covered by a special stratum of coelomic mesothelium, four to five cells in depth. During the 7th week, cells of the superficial stratum invade the original condensation. Thus the entire substance of the spleen is derived from tissues of mesogastric origin. Reticular tissue develops in its substance ; in the spaces of this tissue, large lymphoid cells appear at an early date. The reticular tissue is

permeated by fine branches of the splenic artery. This artery is one of the vessels of the mesogastrium (Fig. 343); its branches end in the developing tissues of the spleen and greater curvature of the stomach. The splenic blood spaces are formed during the earlier part of the 3rd month by dilatation of the capillaries, and perhaps also from veins which, in the developing spleen, are lined by columnar cells. The trabecular and muscular tissues, and the capsule, are derived from the mesoderm of the dorsal mesogastrium. Small masses of splenic tissue (accessory spleens) are occasionally formed in the dorsal mesogastrium near the hilum of the spleen. In lower mammals the splenic formation spreads backwards until it forms a colic lobe lying in the dorsal mesentery

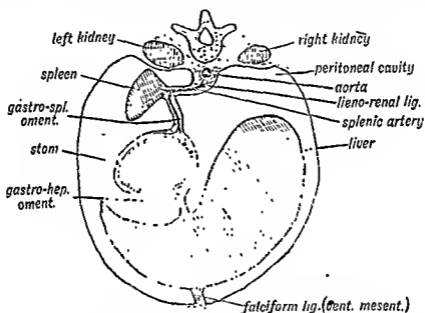


FIG. 343 A diagrammatic transverse section of the Mesogastrium viewed from behind

of the hind-gut [17]. In the 3rd month the surface of the spleen is nodular and deeply incised; about the middle of foetal life the fissures begin to disappear; only on the anterior or gastric border do they persist. The spleen differs from a lymph gland in that its spaces are formed by dilatations of blood capillaries in place of lymph capillaries. The endothelial cells that line the blood spaces and the reticular cells that support the endothelial cells seem to be of the same nature, both adding to the blood a kind of white corpuscle, known as histiocytes [18]. Lymphoid nodules appear in the spleen about the 6th month. Lymphoblasts appear in the blood spaces of the spleen in the 4th month. Presently these give rise to erythroblasts, myeloblasts, megakaryocytes. In the later months of foetal life red corpuscles are formed and so are lymphocytes. The development of the spleen in the mesogastrium

and the termination of its blood in the portal circulation suggest that the spleen is concerned in some way with digestion [19]. It certainly serves as a blood reservoir (Barcroft).

The *gastro-splenic ligament* or omentum is that part of the dorsal mesogastrium which unites the spleen to the stomach (Figs. 340 and 343). It becomes elongated and stretched as the stomach rotates and as the greater curvature is developed. The spleen comes to lie against the posterior (right) surface of the cardiac end of the stomach. The dorsal part of the mesogastrium between the roof of the coelom and the spleen becomes the *lieno-renal ligament*. The rotation of the stomach also leads to the spleen being thrust towards the left side; the dorsal or renal surface of the spleen becomes applied to the peritoneum covering the anterior surface of the left kidney and supra-renal body (Fig. 343). The part of the mesogastrium between the spleen and oesophagus adheres to the diaphragm and forms the *lieno-phrenic ligament*. The manner in which the dorsal mesogastrium becomes applied and adherent to the posterior wall of the abdomen during the 2nd and 3rd months will be described in connection with the secondary attachments of the peritoneum and mesenteries (see p. 403). Minor folds of peritoneum are frequently formed between the spleen and great omentum [20].

The Pancreas [21].—The pancreas appears in the latter part of the 4th week of development as two outgrowths from that part of the fore-gut which becomes the duodenum. The pancreatic buds develop within the ventral as well as within the dorsal mesentery for, at their points of origin from the duodenum, these two mesenteries are in continuity (Fig. 340). Of the two buds one is a minor process which springs from the ventral aspect of the duodenum in common with the hepatic diverticulum (Fig. 344, *A*). The ventral bud is usually double [22], but in man the left outgrowth commonly atrophies, while the right goes on to form part of the head of the pancreas (Fig. 344, *B*). The duct of the right ventral bud becomes the terminal part of the main pancreatic duct (duct of Wirsung); the ventral bud forms the lower part of the head of the pancreas and the process that projects behind the portal vein (uncinate process) [23]. The greater part of the pancreas is formed by the dorsal bud that arises from the duodenum nearer to the pylorus than the hepatic outgrowth [24]. It grows into the dorsal mesogastrium, towards the spleen (Fig. 340). The rotation of the stomach, the migration or displacement of the duodenum towards the right side of the abdomen, with a developmental rotation in the wall of the duodenum, bring about, during the 6th and 7th weeks, a displacement of the termination of the common bile duct and of the ventral pancreas to the inner or mesial side of the duodenum, the ventral pancreas being thus

brought in contact with the dorsal pancreatic outgrowth (Fig. 344, *B*). In animals in which both right and left ventral outgrowths of the pancreas persist, the left may send a process within the gastro-hepatic omentum, round the bile duct, almost to the transverse fissure of the liver. A representative of this omental lobe is occasionally present in man (Fig. 345). The ducts of both processes may persist, the duct of the dorsal bud (duct of Santorini) opening half an inch above the opening of the bile duct; the duct of the ventral bud (Wirsung's) terminates with the common

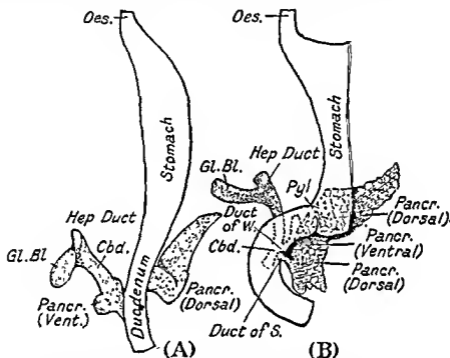


FIG. 311

- A.* The Hepatic and Pancreatic Buds arising from the terminal part of the Fore-gut Stage reached in the 5th week.
B. The stage reached in the 7th week. The duodenal loop has migrated towards the right, while the termination of the bile duct and "ventral bud" of the pancreas have moved to the inner or medial side of the duodenum.
Cbd., common bile duct; *Hep. Duct*, hepatic duct (stalk of liver bud); *Gl. Bl.*, gall bladder; *duct of W.*, duct of Wirsung; *duct of S.*, duct of Santorini.

bile duct (Fig. 345). The terminal part of the duct of Santorini commonly becomes obliterated and the secretion of the dorsal pancreatic outgrowth finds a new exit through an anastomosis between its duct system and that of the ventral bud, which is effected in the 3rd month. Even if the duct of Santorini persists, the secretion from the dorsal bud reaches the duodenum mostly through the duct of the ventral bud—the duct of Wirsung. Occasionally the duct of Wirsung does not join the common bile duct, but opens separately in the duodenum.

The Vaterian Ampulla.—During the latter half of the 8th week, while the lumen of the second part of the duodenum is occluded by an

endodermal proliferation, changes are taking place in the intra-intestinal (terminal) part of the common bile duct and in the corresponding part of the duct of the pancreas. Their common opening becomes produced into an elevation within the duodenum, the duodenal papilla [25]. On this papilla the ducts open. In Fig. 346, *A*, is shown a section of the papilla at the end of the 8th week; the ducts are seen to meet in a common terminal passage—the ampulla of Vater—within the papilla. In more than 50% of adults the ampulla is divided by the partition (x), between the bile and pancreatic passages, reaching the apex of the papilla. A circular sphincteric musculature (sphincter of Oddi) is developed, not only round the terminal ducts but also round the ampulla.

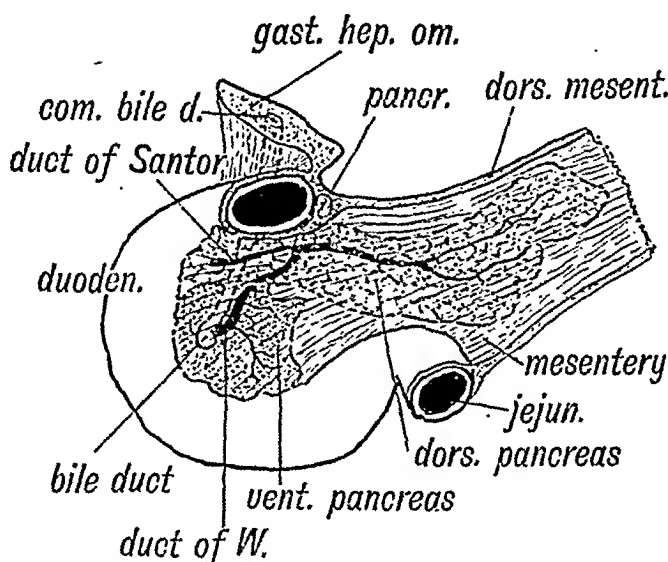


FIG. 345. Diagram of the Pancreas showing (1) its primary relationship to the Dorsal and Ventral Mesenteries; (2) the parts formed from the Ventral and Dorsal Outgrowths; (3) the Formation of the Duct of Wirsung (duct of *W.*) by a union between the Ducts of Dorsal and Ventral Buds.

It appears in the 7th week, and is developed out of the mesenchymal coats of the ducts.

The developing pancreatic process is at first hollow, like the primary liver process, but the secondary outgrowths are solid and cylindrical. They divide and redivide, acquire lumina, and form an acino-tubular gland. About the end of the 3rd month some of the acini, particularly in the tail of the pancreas, already distinguished by the staining reaction of their cells, become partially or entirely separated from the duct-system and form the *islands of Langerhans* [26]. They can be recognized by the naked eye in the pancreas of certain fishes and removed by knife and forceps. The semi-isolated acini, of which there are several hundreds, are found in all parts of the pancreas, and represent the first stage in the separation of an ordinary duct gland into two elements—

one producing an external secretion, the other a highly important internal secretion. We see from the example of the pancreas how ductless glands like the thyroid and pituitary may have arisen from duct glands by atrophy of the excretory part. The capsule and connective

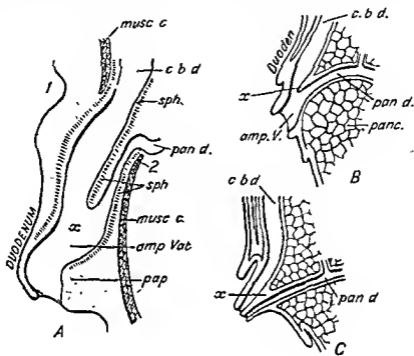


FIG 346.

1 Section along sphincter—muscle of the

C Where there is no ampulla, the partition (x) being prolonged to the apex of the papilla.

tissue of the pancreas are derived from the mesoderm of the dorsal mesentery.

Relationship of the Pancreas to the Peritoneum and Vessels.—1. *In the Embryo.*—The pancreas develops between the layers of the dorsal mesogastrium, just where this structure is being expanded to form the wall of the omental sac (Fig. 341). From the first it is completely surrounded by peritoneum, and it lies with its tail directed forwards against the spleen and its head in the dorsal bend of the *duodenal loop* (Fig. 347). It comes to lie parallel to the great curvature (dorsal border) of the stomach. In Fig. 347 a schematic drawing is given of the essential relationship of the pancreas to the dorsal mesogastrium in lower vertebrate animals; it also represents the condition to be seen in a human

embryo during the 5th week of development, when the dorsal mesentery is swollen with young tissue and attached along the mid-dorsal line. The coeliac axis is the artery of the mesogastrium and of the structures that it contains ; it may be described as the artery of the fore-gut. The coronary artery passes direct to the cardiac end of the stomach ; the splenic is a short vessel ending on the cardiac dilatation of the stomach, and supplying the spleen ; the hepatic passes on the right side of the pancreas to the duodenum and pyloric end of the stomach, and ends in the liver by passing through the ventral mesentery. As the stomach

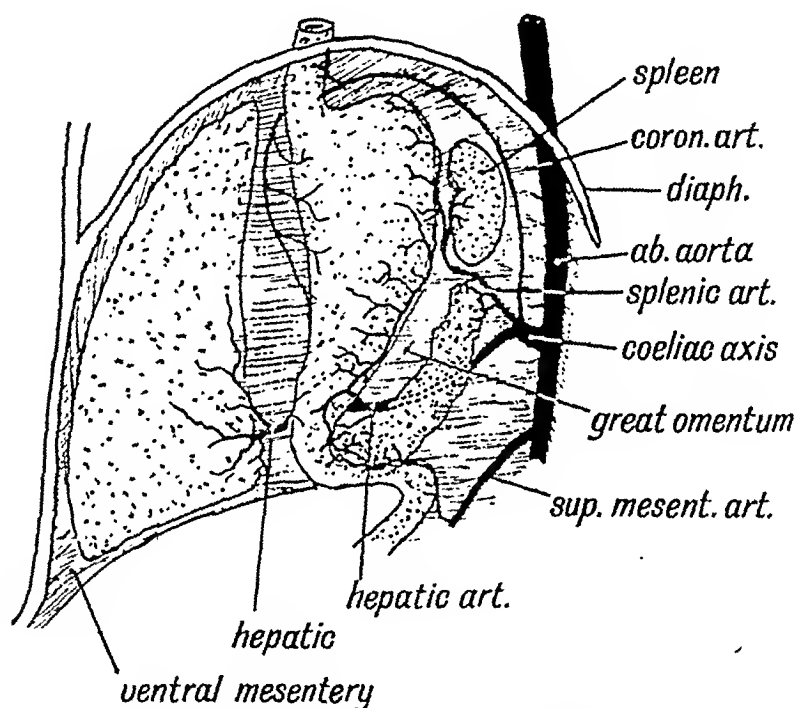


FIG. 347. Schematic representation of the Dorsal Mesogastrium and its contents.

migrates backwards during the 6th and 7th weeks, the origin of the coeliac axis moves also.

2. *In the Adult.*—The development of the great omentum and the rotation of the stomach to the left, lead to the pancreas being pressed against the left side of the posterior wall of the abdomen. That part of the dorsal mesogastrium which lies between the stomach and pancreas becomes elongated enormously, during the 3rd and 4th months, to form the *great omentum*, and hence the two anterior layers of the great omentum are attached to the great curvature of the stomach and to the gastrosplenic omentum (Figs. 347, 348). The two posterior layers of the omentum end on the lower (formerly ventral) border of the pancreas. The great omentum is well developed in all mammals, its origin being probably related to that of the diaphragm. Its exact function is

unknown, but it is connected with respiratory movements, with the absorption, and perhaps also with the secretion, of peritoneal fluids; it is a great phagocytic mechanism. The duodenal loop, with the head of the pancreas in its concavity, is also pressed against and becomes closely attached to the posterior abdominal wall. During all the changes which take place in the position of the pancreas and spleen, owing to the rotation of the stomach and intestine, one structure remains fixed, and that is the coeliac axis. The part of the mesogastrium in which the spleen and tail of the pancreas are situated becomes greatly drawn out. Both structures, instead of being situated near the middle line dorsal to the stomach, are moved to a position in front of the left kidney, the

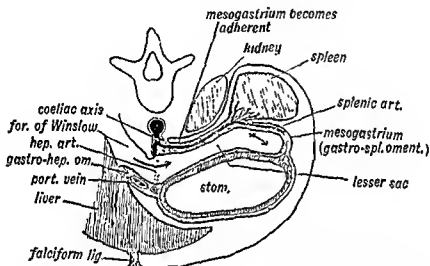


FIG. 348. Diagram to show the Formation of the Lesser Sac of the Peritoneum from the Dorsal Mesogastrium. The arrow lies in the isthmus between the vestibular and omental parts

pancreas thus coming to lie across, instead of along, the abdominal cavity. The mesogastrium is ballooned out towards the left side to form the lesser sac of the peritoneum, and as the splenic artery lies in the mesogastrium it also is drawn towards the left, circumventing the lesser sac of the peritoneum (Figs. 341, 348).

Up to the 7th week of embryonic life the pancreas lies between the layers of the dorsal mesogastrium and the extension from these layers which forms the mesentery of the duodenal loop; thus right and left surfaces are covered by peritoneum. The left surface, which becomes anterior, retains its covering, but during the 6th week the right aspect of the pancreas and duodenal loop become applied to the posterior abdominal wall in front of the aorta, crura of the diaphragm and left kidney (Fig. 348). The peritoneal covering on the right aspect gradually disappears, and thus in the adult the pancreas comes to appear as if it

embryo during the 5th week of development, when the dorsal mesentery is swollen with young tissue and attached along the mid-dorsal line. The coeliac axis is the artery of the mesogastrium and of the structures that it contains ; it may be described as the artery of the fore-gut. The coronary artery passes direct to the cardiac end of the stomach ; the splenic is a short vessel ending on the cardiac dilatation of the stomach, and supplying the spleen ; the hepatic passes on the right side of the pancreas to the duodenum and pyloric end of the stomach, and ends in the liver by passing through the ventral mesentery. As the stomach

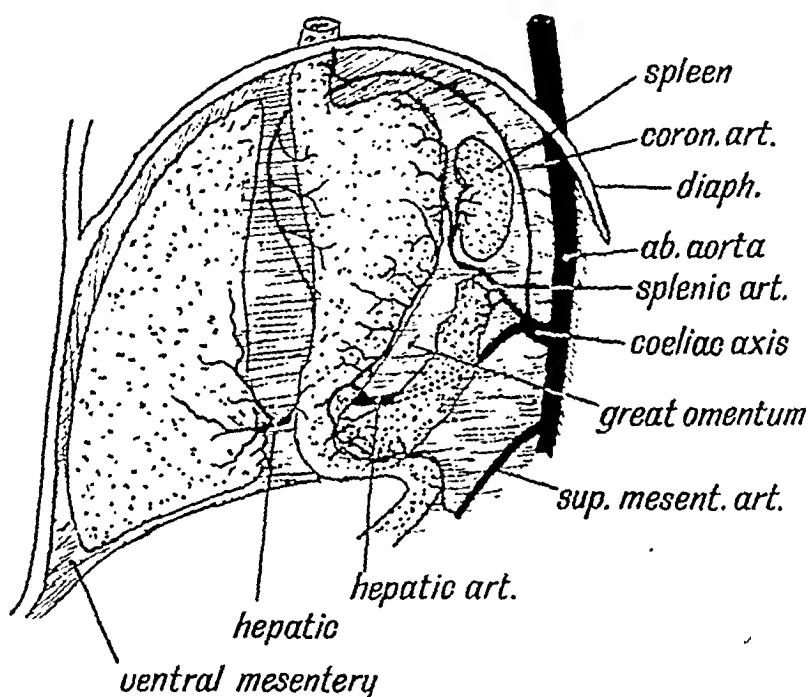


FIG. 347. Schematic representation of the Dorsal Mesogastrium and its contents.

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- [12] For morphology of liver, see Thomson, A., *Jour. Anat.*, 1899, 33, 546; Thompson, P., *ibid.*, 1914, 48, 222; Keith, Sir A., *Lancet*, 1903, 1, 631, 709.
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- [25] For development and musculature of the terminal parts of bile and pancreatic ducts, see Schwegler and Boyden, *Anat. Rec.*, 1937, 67, 441; 1937, 68, 17, 193; Kreilkamp and Boyden, *ibid.*, 1940, 73, 485 (sphincter of Oddi); Kirk, John, *Jour. Anat.*, 1944, 78, 118 (histology of the ampulla); Dardinski, V. J., *ibid.*, 1935, 59, 469 (ampulla is completely divided in 51% of cases); Gregoire, R., *Ann. Anat., Path.*, 1934, 11, 208, 321; Weissberg, H., *Anat. Anz.*, 1935, 79, 321 (annular pancreas).
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- [27] Crymble, P. T., *Jour. Anat.*, 1913, 47, 207; see also references to Frazer, J. E., note [1]; to Broman, I., note [2]; to Keith, Sir A., note [12].

lay behind and outside the cavity of the peritoneum. The complete application and fixation of the pancreas and duodenum to the posterior abdominal wall only occur in animals adapted to the upright posture (see Figs. 335, 336, 348). The part of the dorsal mesogastrium between the pancreas and aorta (Fig. 348) is also applied to the posterior abdominal wall, and forms the posterior lining of the lesser sac.

The *Lesser Sac* (*Bursa Omentalis*) is composed of two parts, a vestibular or hepatic part formed from the recessus mesentericus (Figs. 335, 336); and an omental or gastric part formed by the evagination of the dorsal mesogastrium. These two parts communicate at an isthmus or constriction caused by the coronary and hepatic arteries (Fig. 348). The hepatic recess or pocket separates the Spigelian lobe of the liver from the right crus, and permits the liver to glide during the respiratory movements of the diaphragm (Figs. 334, 336). The gastric part isolates the stomach, allows it to contract, expand and move during digestion and respiration. In the anterior wall of the lesser sac are situated (Fig. 348): (i) the gastro-hepatic omentum or ventral mesentery, which is at first vertical and median; (ii) the stomach; (iii) the gastro-splenic omentum, a part of the dorsal mesentery; (iv) the two anterior layers of the great omentum, also parts of the dorsal mesentery. In its posterior wall are situated: (i) the lieno-renal ligament (dorsal mesentery); (ii) the dorsal mesentery of pancreas; (iii) two posterior layers of the great omentum [27].

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dorsal to the root of the mesentery of the small bowel. It will be observed that the duodenal loop has been rotated to the right; irregularities of rotation occur [2]. The superior mesenteric artery thus comes to pass in front of (ventral to) the terminal part of the duodenum. The fixation of the duodenum is but one of a series of most complicated plastic operations carried out in the human abdomen by cells of the peritoneum during the 3rd and 4th months of development. Such operations are so important that we must look at them more closely.

Process of Peritoneal Fixation.—We have seen that certain developmental processes, such as the obliteration of the embryonic clefts of the lip and of the palate, or the union of the medullary folds to enclose the neural tube, are akin to the processes that lead to the union of the lips of a wound made by a surgeon's knife (p. 240). In the peritoneal cavity we are to see examples of another process with which surgeons are familiar—the formation of adhesions that follow inflammatory disturbances of the peritoneum [3]. The passages that lead from the pericardium to the pleura, from the pleura to the peritoneum and from the peritoneal cavity to the tunica vaginalis of the testes, are closed by the formation of developmental adhesions. The peritoneal adhesions with which surgeons are familiar follow inflammation, but the developmental process—the process of *zygosis*—which leads to the adhesion of the mesentery of the duodenum and part of the mesogastrium to the dorsal wall of the abdomen in the latter part of the 2nd month of embryonic life, are not preceded by inflammatory changes, but are the result of a growth process arising from an unknown stimulus. The process of *zygosis* is active not only in foetal life but is also to be seen at work at, and even after, birth, particularly in the mesosigmoid. The applied peritoneal surfaces become adherent by the proliferation and union of lining cells of the opposed layers of peritoneum. The adhesions, as they form, contract and thus draw the various parts of the alimentary canal to their final position, much in the same way as the testes come to be lodged in the scrotum. We are here dealing with growth manifestations utilized for a mechanical purpose. The secondary adhesion of the mesenteries of the abdominal viscera are apparently related to posture; the degree of adhesion is much more extensive in man than any other animal, with the exception of the great anthropoid apes. Man and the anthropoids are distinguished from all other animal forms by the upright posture of their bodies. The peritoneal adhesions that occur from the middle of the 2nd month onwards must be regarded as adaptations to the upright posture. The suspensory ligament of the spleen, the right and left *costo-colic* ligaments, the peritoneal bands passing from gall bladder to the colon or omentum are of the same nature, and are formed

CHAPTER XXI

ORGANS OF DIGESTION (continued)

THE MID- AND HIND-GUT

The *duodenum* is made up from the terminal part of the fore-gut and the first part of the mid-gut. It serves as the pace-maker for the peristaltic movements of the whole of the small bowel and it is probably for this reason that muscle becomes differentiated earlier in the wall of the duodenum than in any other part of the small intestine, the circular coat appearing in the 7th week (Frazer). The stage of differentiation and the area of fixation of the duodenum in the 9th week of development are shown in Fig. 349. The derivatives of the mid-gut at this time still

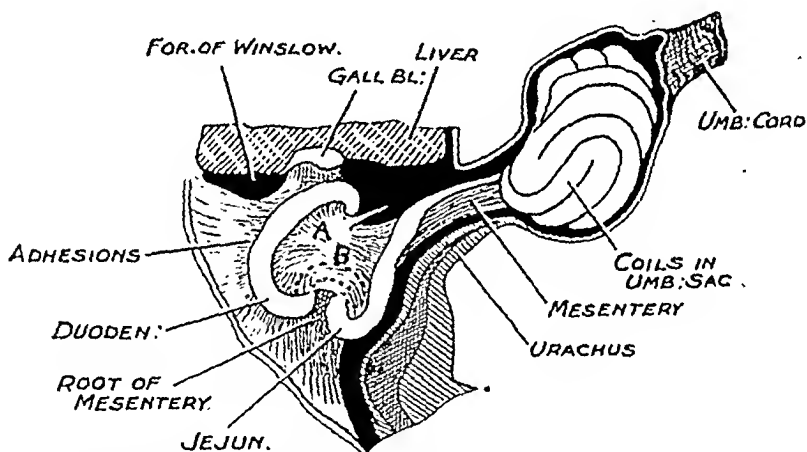


FIG. 349. The Fixation of the Duodenum in the 9th week just before the return of the Intestines from the Umbilical Sac. (After Prof. J. E. Frazer.)

A, on mesoduodenum near remnant of vitelline vein; B, indicates buried duodeno-jejunal junction.

lie within the umbilical cord. The duodenum is being fixed in position by active operations carried out by the mesenchyme of the peritoneum and mesenteries. Mesenchyme cells in the neighbourhood of the duodenum are effecting the following attachments (Fig. 349): (i) retro-duodenal adhesions which fix the duodenal loop to the dorsal wall of the abdomen; (ii) adhesions between the first part of the duodenum and liver—often involving the gall bladder; (iii) most important of all—a “retention band” binds the termination of the duodenum and beginning of the jejunum (duodeno-jejunal angle) to the root of the primitive mesentery—near the point where the coeliac axis arises from the aorta [1]. As will be seen in Fig. 349, the duodeno-jejunal angle lies behind or

(i) The production of the mid-gut as a U-shaped loop. (ii) The formation within the umbilical cord of a long neck to the yolk sac—the *vitello-intestinal duct*; Meckel's diverticulum is formed by a persistence of the intra-abdominal part of the canal. Normally the duct becomes occluded, and shrivels up during the 6th week; this is the case in all mammals, but in birds the yolk sac is large at the time of hatching, and part of it always persists as an intestinal diverticulum. (iii) The yolk sac, by the constriction of the umbilical orifice and formation of the cord, comes to lie on the placenta, where a remnant of it may be found at birth near the implantation of the cord (Fig. 350).

Vessels of the Yolk Sac.—Although at first the yolk sac receives a series of branches from the aorta, by the time of its separation from the mid-gut the number has been reduced to one—the superior mesenteric, which becomes the artery of the U-shaped loop (Fig. 350). Its vein, however, the left vitelline, has no connection with the superior mesenteric vein, but when the U-shaped loop is formed, continues its original course and ends in the portal vein at the lower border of the pylorus (Figs. 349, 353). When the vitello-intestinal duct atrophies in the 6th week, the same fate overtakes the vessels of the yolk sac, but they too may persist as cords.

Umbilical Coelom and Intestinal Loop.—At first the coelom extends into the proximal segment of the umbilical cord and it is within this umbilical recess of the peritoneal cavity that the U-shaped loop—the mid-gut—undergoes its earlier developmental changes. The structural features of the loop are shown in Fig. 350; it is made up of a proximal or jejunal limb and of a distal or colic limb, for already in the 6th week, when the embryo is little more than 5 mm. in length, the caecal diverticulum is apparent. In Fig. 351 a dissection of the intestinal loop is shown, from an embryo late in the 6th week of development. Already the process of rotation has commenced—the jejunal limb coming to lie to the right and behind or dorsal to the colic limb. The mesoduodenum is becoming adherent to the dorsal wall (Fig. 351), while, as Prof. Frazer has shown, certain "traction bands" are forming within the common mesentery and thus guiding and regulating the movement and fixation of the loop. The condition in the 9th week is shown in Fig. 352; within the umbilical coelom coils of small intestine have been produced from the jejunal and ileal parts of the loop; also a jejunal coil within the abdomen from the proximal limb. The duodeno-jejunal flexure is now closely bound to the dorsal wall by traction bands—part of which become muscular and form the *Muscle of Treitz* [5]. Then, suddenly, in the 10th week, when the foetus is about 42 mm. long, the loop is retracted within the abdomen and the umbilical recess becomes closed. Sometimes the sac of peritoneum in the cord is also drawn within the abdo-

by secondary adhesions of the peritoneum in the later months of foetal life [4].

The Mid-Gut.—The mid-gut extends from the Vaterian or biliary orifice in the duodenum almost to the splenic flexure of the transverse colon. Its artery is the superior mesenteric. To understand the strange manner in which the mid-gut is developed—as a loop within the base of the umbilical cord—it has to be remembered that part of the small bowel arises precociously to form a yolk sac for the nourishment of the embryo and that a corresponding part of the belly-wall has been modified to form the chorion and amnion (p. 35). The umbilical cord represents a

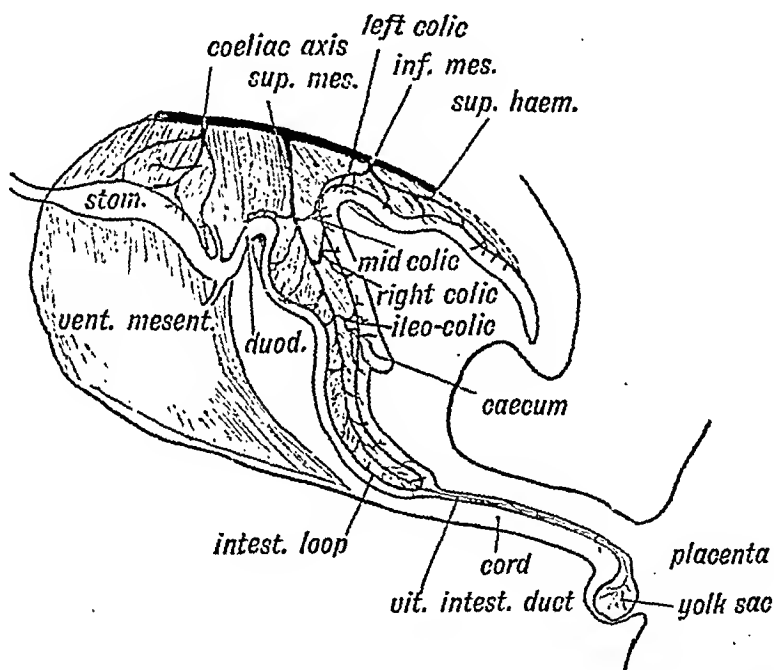


FIG. 350. Schematic representation of the Alimentary Canal, and of its Mesenteries and Arteries during the 6th week of development.

modified part of the body-wall. It is not therefore against the natural order of things that the mid-gut, when it is formed, comes to lie as a loop within the coelom or peritoneal cavity of the umbilical cord.

Yolk Sac and Meckel's Diverticulum.—The yolk sac reaches its maximum size in the later part of the 4th week, when its neck, filling the embryonic umbilicus, extends from the septum transversum in front to the allantois behind (Fig. 322). In the 5th week (Fig. 323) the mid-gut has become a V-shaped tube; the yolk sac, now lying in the umbilical cord, which is just beginning to be differentiated, is joined to the apex of the mid-gut by a stalk or neck. The condition reached in the 6th week is shown diagrammatically in Fig. 350. The following points are to be noted :

varies in length and shape; its blind end is frequently hulous and the site of secondary diverticula. Occasionally pancreatic masses are developed at its extremity. It is lined by a glandular epithelium similar to that of the ileum. Frequently a fold of the mesentery descends to it (Fig. 354). In the mesenteric fold there is usually to be found a vestige of the artery of the yolk sac (Fig. 350). The attached base of the mesenteric fold may atrophy, while the free margin forms a cord, under which a loop of bowel may become strangulated (Fig. 354).

(ii) The vitello-intestinal duct may remain patent, and, when the cord is cut at birth, form a fistulous opening at the umbilicus, by which the contents of the ileum escape. A part may become grafted on the umbilicus, giving rise to the condition known as "weeping navel"

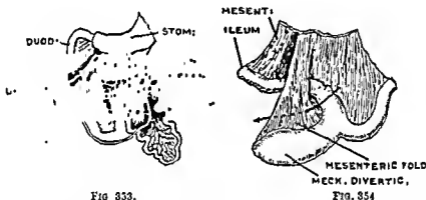


FIG. 353.

FIG. 354

FIG. 353 Fibrous remnants of the Artery (a) and Vein (b) of the Yolk Sac of a Kitten

FIG. 354 Meckel's Diverticulum provided with a Mesentery The arrow marks the site at which the aperture may be formed in the mesenteric fold

(Stiles). Or the mucous membrane thus grafted may assume the structure of the lining membrane of the stomach [9].

(iii) The artery of the yolk sac, representing the terminal part of the superior mesenteric, may persist as a fibrous band, which stretches from the mesentery at the situation of a Meckel's diverticulum to the umbilicus. Over such a cord the gut may become strangulated. The young of all carnivora are born with thread-like remains of both artery and vein, stretching between the mesentery and the umbilicus. A remnant of the vein may persist in the human subject; the cord in such cases joins the mesentery below the head of the pancreas (see Fig. 349). The vitello-intestinal duct may also be reduced to form a cord, over which a loop of intestine may fall and thus become strangulated.

(iv) The U-shaped loop, instead of retreating within the abdomen early in the 3rd month, may remain within the umbilical recess. This gives rise to a congenital umbilical hernia. Such herniae occur in all degrees; they may contain merely a loop of bowel or almost the whole of the

men [6]. We must regard the withdrawal as due to the action of "contraction" or "retraction" bands in the mesentery. During the weeks spent by the intestinal coils in the umbilical recess, the lung buds are expanding and the pleural cavities and diaphragm are being formed, and the safeguarding of these processes may be the reason for an extra-abdominal development of the intestinal loop [7]. More particularly it has to be noted that in the 3rd month the abdominal cavity becomes enlarged by the elongation of the lumbo-sacral segment of the spine (see p. 420). Further, the operation of rotation of the bowel, necessary

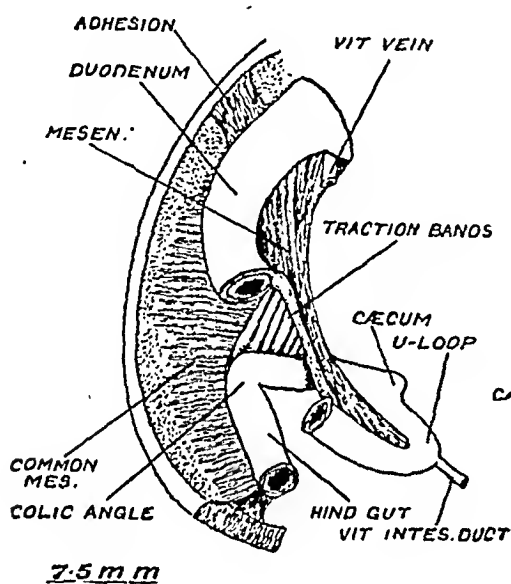


FIG. 351.

FIG. 351. The Intestinal Loop, seen from the right side, in an Embryo in the 6th week of development. (Prof. Frazer.)

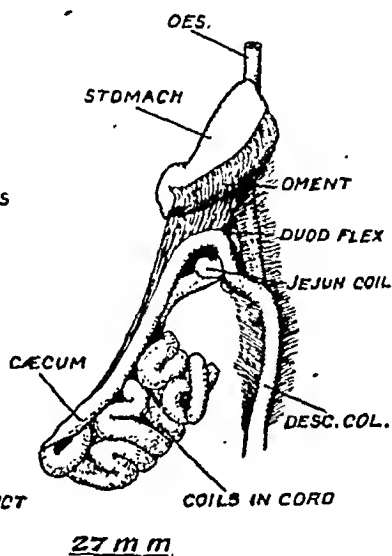


FIG. 352.

FIG. 352. The Intestinal Loop, within the Umbilical Coelom, of a Foetus in the 9th week, seen from the left side. (Prof. Bardeen.)

for its fixation, is facilitated by the bowel being shaped as a loop and by the loop being placed within a special recess of the peritoneum.

Persistence of Certain Embryonic Structures.—Many of the structural features seen in the human embryo at the stage of development reached during the 5th and 6th weeks may persist [8].

(i) The most common structure to remain is the intestinal end of the neck of the yolk sac—*Meckel's diverticulum*. It occurs in 2% of subjects, and commonly forms a finger-like sac on the free border of the ileum from 2 to 4 feet above the ileo-caecal orifice. Hence we know that this part of the ileum forms the apex of the U-shaped loop of intestine. The point on the ileum at which the canal of the yolk sac was attached is frequently the seat of a narrowing, which may be more or less marked. At this site intussusception of the bowel may occur. The diverticulum

(Lewis and Thyng). As may be seen from Fig. 346, *A*, there is a gap in the muscular coat of the duodenum through which the bile and pancreatic ducts enter. Diverticula of the mucous coat may occur through this gap; such diverticula are not developmental in origin [11].

Congenital Occlusion of the Duodenum.—The part of the duodenum just above the opening of the bile and pancreatic ducts may be partially or completely closed in newly born children (Fig. 355). After the liver and pancreatic buds grow out, this part of the duodenum becomes occluded by the proliferation of its lining epithelium—and the lumen remains blocked during the 5th and 6th weeks [14]. The epithelium instead of becoming absorbed may become organized, an occlusion being thus produced. Such cases are not rare [15]. A proliferation of

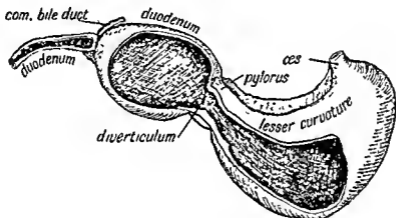


FIG 355. Congenital Occlusion of the Duodenum

the lining epithelium, with arrest of expansion of the lumen, may occur at many points of both jejunum and ileum [16].

We have just seen (p. 406) that the duodeno-jejunal junction becomes sharply bent behind the root of the mesentery and is there fixed to the posterior abdominal wall by a strand or band developed within the mesentery (Fig. 352). This band, which contains non-striated muscular fibres, ends in the right crus of the diaphragm. This *suspensory band*, usually known as the muscle of Treitz, renders the duodeno-jejunal junction the most fixed part of the intestinal tract [17].

DERIVATIVES OF THE HIND-GUT

At the beginning of the 2nd month the hind-gut is almost equal in length to the mid-gut, but its calibre is less. Indeed, it is not until the 5th month that the hind-gut is marked off from the mid-gut by having a greater diameter. By the end of the 2nd month, as we have just seen, the anterior (jejunal) limb of the intestinal loop has grown very

movable contents of the abdomen. In all cases the wall of the hernia is thin and transparent.

Differentiation of the Coats of the Intestinal Wall.—In the 6th week the small intestine has a diameter of less than a millimetre and measures only 4 mm. in length [10]. It is lined by low cuboidal endoderm resting on a coat of mesenchyme. In the mesenchymal tissue the circular coat of muscle begins to be differentiated in the 6th week, appearing first at the duodenal end, and spreads from there towards the ileo-caecal junction. The outer or longitudinal coat appears a month later. By the end of the 2nd month the small intestine has become 36 mm. long; in the full-time child its length is about 300 cm.; from these measurements we learn how rapidly the small intestine grows in length and how quickly its cellular elements multiply. In the 3rd month villi begin to form, again in a proximo-distal direction. A little later the crypts or glands of Lieberkuehn are developed between the villi; they keep on increasing in number until after birth. Bruenner's glands appear in the duodenum in the 3rd month.

Lymphoid follicles are recognizable in the mucous coat in the 4th month and Peyer's patches in the 7th, but these are not apparent to the naked eye until a month after birth. Valvulae conniventes are formed in the 8th month, thus increasing the area of absorption. They appear first in the distal part of the duodenum; their development fades as the ileum is approached.

Between the outer longitudinal and inner muscular coats there is a cellular zone in which new muscle fibres seem to arise. It is in this zone, too, that nerve cells are found, from which Auerbach's plexus is developed. These cells are derived from the neural crest, for if the crest is removed from the embryonic cord, no nerve cells are found in the intestinal wall. The power of differentiation is inherent in the embryonic intestine, for if a segment is excised from a foetal rabbit and grafted on the omentum of an adult animal, its various coats will become differentiated [10].

Congenital Diverticula.—During the 3rd month numerous outgrowths of intestinal epithelium take place; they perforate the muscular coats [11]. They are usually absorbed, but they may give rise to diverticula, a common site being at the ileo-colic angle. At this site the orifice of the diverticulum may become closed, a cyst being thus formed [12]. Congenital diverticula and cysts are distinguished by possessing all the intestinal coats. Part of the bowel may become duplicated or divided longitudinally during development, one compartment assuming the appearance of a long diverticulum [13]. Often masses of pancreatic tissue are attached to congenital diverticula

intestines are drawn within the abdominal cavity they tend to press the descending meso-colon against the parietal peritoneum covering the left kidney (Fig. 357). The left layer of the meso-colon adheres by the process of zygosis to the pre-renal layer of the peritoneum, both layers subsequently being absorbed. Thus the descending meso-colon, originally situated in the middle line, comes to be attached in the left lumbar region by adhesions that form during the 5th, 6th and 7th months (Fig. 357).

Intersigmoid Fossa.—The sigmoid flexure, which is made up of the pelvic colon and part of the iliac segment, after the rotation of the gut, forms a loop, with its convexity directed towards the liver. The sigmoid flexure or loop is not differentiated until late in the 4th month. Its late appearance in the human foetus is probably due to the fact of its recent evolution, for it is found only in the higher primates. In nearly

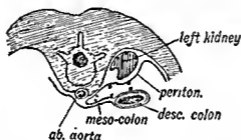


FIG 357 Diagram to show how the descending Meso-colon becomes applied to the Parietal Peritoneal of the left Lumbar Region

20% of human foetuses it is not differentiated, the primitive form being retained (Toenbury). On the other hand, in more than 10% of people there is an over development, there being a double loop. The position of the sigmoid loop is most variable; in 20% of people it reaches the right iliac fossa [18]. The meso-sigmoid is originally attached in the middle line, but the pressure of the developing loops of small bowel brings it against the posterior abdominal wall and left iliac fossa. The mesentery of the sigmoid may become completely adherent like the descending meso-colon, or only partially. When the sigmoid is lifted up a recess or fossa may be apparent beneath the meso-sigmoid, to the outer side of the left common iliac artery, which is due to a failure of adhesion between the meso-sigmoid and parietal peritoneum. It occurs opposite the convexity of the sigmoid loop (Fig. 336). At birth the meso-sigmoid is relatively extensive; the sigmoid loop lies with its convexity towards the right side of the abdomen and well above the pelvis. During adolescence the sigmoid grows more slowly than the rest of the colon. It sinks within the pelvis, and forms the greater part of what has come to be named pelvic colon.

rapidly, and become thrown into a number of distinct loops. At birth the small intestine is six times the length of the large bowel.

The *rectum* is formed out of the posterior end of the hind-gut. The manner in which the rectum is separated from the cloaca, the anal canal formed and the permanent anus produced will be described in connection with the perineum and urogenital passages, for their history is closely associated with the development of these structures (see p. 534).

The *descending, iliac and pelvic segments of the colon* are also formed out of the hind-gut. The artery of the hind-gut is the inferior mesenteric (Fig. 356). Hence it supplies the rectum, sigmoid and descending colon.

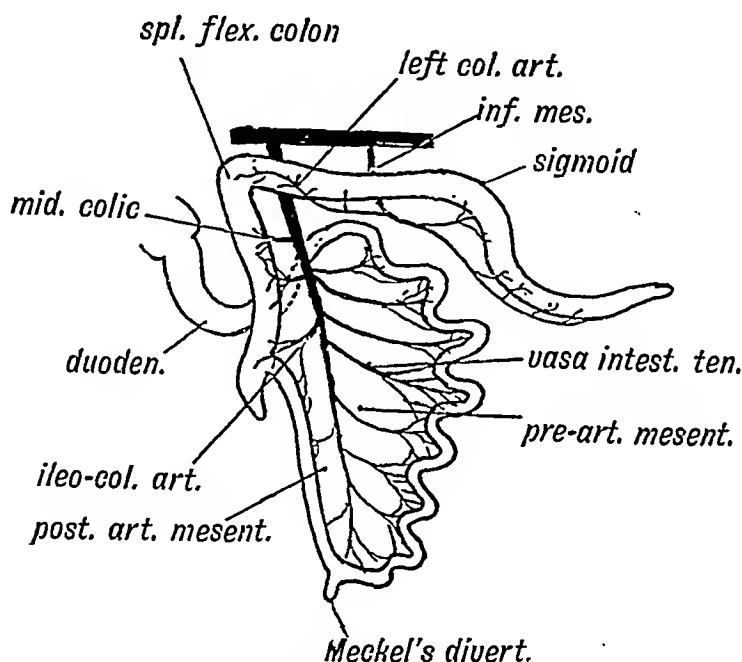


FIG. 356. The Mesentery of the Hind-gut. The position assumed by the colon after the rotation of the gut has taken place.

In the 6th week the hind-gut is suspended from the front of the aorta and spine by the dorsal mesentery of the hind-gut (Figs. 350, 351). This becomes transformed into the meso-rectum, meso-sigmoid and descending meso-colon. The angle between the hind-gut and U-shaped loop (Fig. 351) becomes merged into the terminal part of the transverse colon, the splenic angle being undifferentiated until the 4th month (Frazer). Early in the 3rd month, when the intestine takes up its permanent position within the abdomen, the U-shaped loop has become twisted round on the axis of the superior mesenteric artery (Fig. 356), so that the part of the hind-gut which will form the splenic flexure is turned forwards and to the left, assuming ultimately the position shown in Fig. 365. It carries its artery, the left colic, with it. When the small

undergoes a great reduction in size and growth when the period of adolescence is past. Thus there are five structures to be observed in the ileo-colic region of a typical mammal (Fig. 358): (i) an ileo-colic sphincter; (ii) a caeco-colic sphincter; (iii) a caecal segment of the colon; (iv) a caecum, the distal part of which may be specialized to form (v) an appendix. Further, a study of the comparative anatomy of this region shows that the caecum is largest in vegetable-feeding animals, and that there is a correlation between the development of the stomach and caecum. In the horse, for instance, the caecum and caecal colon are complicated, the stomach simple; in the ruminants the stomach is complex, the caecum comparatively simple. In animals which live on a flesh diet the caecum is small.

The development of the ileo-caecal sphincter in the howel of the human

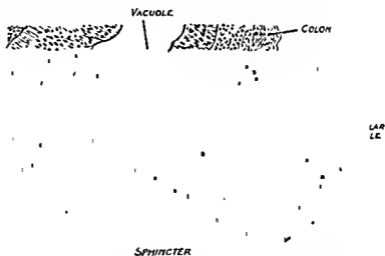


FIG. 359. Section through the ileo-caecal Junction of a Foetus 32 mm. in length. (Prof. J. Beattie)

embryo has been studied by Prof. John Beattie [21]. In Fig. 359 is represented a section of the ileo-caecal junction of a foetus which has just entered the 3rd month of development. The circular muscular coat is becoming differentiated; at the junction of ileum and great howel, the muscular coat is seen to be growing inwards to form a special ring or sphincter.

Development of the Colon and Caecum.—Early in the 6th week of development an elevation appears on the free border of the posterior limb of the U-shaped loop (Figs. 350, 351). The elevation contains a diverticulum of the caecal colon, which becomes differentiated to form the caecum and appendix. The caecal diverticulum continues to grow outwards and forwards in close contact with the free border of the ileum, but by the end of the 2nd month the caecal diverticulum is clearly

Morphology of the Ileo-colic Part of the Bowel.—In all vertebrates, from fishes upwards, the junction of the small with the great intestine is demarcated by the *ileo-colic sphincter*, developed from the circular coat of the bowel [19]. As a rare abnormality the caecum may be absent in man, the only external indication of the ileo-colic junction being the presence of the ileo-colic sphincter. This is the normal condition in the frog, and in several mammals such as the racoon. The sphincter marks the junction of two different functional segments of the alimentary tract. Villi, which are originally developed in the great bowel, disappear in the later months of foetal life. The proximal part of the colon from which the caecum is developed forms the caecal colon (Fig. 358) ; it is frequently

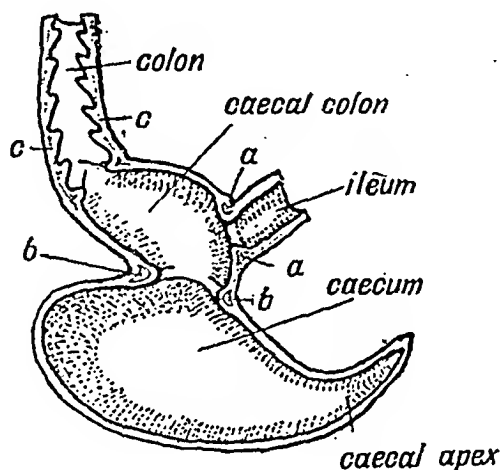


FIG. 358. Diagram to show the parts of a typical Mammalian Caecum. Five parts are shown in the figure : (1) the termination of the ileum ; (2) the caecal colon in which the ileum ends ; (3) the caecum which opens from the caecal colon ; (4) the apex of the caecum ; (5) the commencement of the ascending colon. At three points the circular muscular fibres are thickened to form sphincters : (a) ileo-colic junction ; (b) at the junction of caecum and caecal colon (in man a and b are combined in the ileo-caecal orifice and its retinacula) ; (c) in the first part of the ascending colon.

demarcated from the ascending colon by a thickening of the circular muscular coat—the *caeco-colic sphincter* (Fig. 358, c)—which can commonly be recognized in the bowel of man [20]. The caecum is developed as a diverticulum of the caecal colon. In all vertebrates its submucous coat is rich in lymphocytes, which in mammals collect in the form of solitary follicles more or less closely crowded together. R. J. Berry found that in the primates there is a tendency for the lymphoid tissue to be aggregated in the apex of the caecum. In man, in anthropoids, and a few other forms, the lymphoid tissue becomes richly developed in the distal part of the caecum, which has a narrow lumen, strong muscular coat, and is of great functional activity during digestion. This highly specialized part of the caecum is the appendix ; it is well developed in man, and is certainly not a vestigial structure. The lymphoid tissue

1. The mesentery of the anterior limb, in front of the superior mesenteric artery: forms the *pre-arterial part*. This gives rise to the greater part of the mesentery of the small bowel.

2. The mesentery of the posterior limb, behind the artery: is the *post-arterial part*. It forms the mesentery of the ascending and transverse colon, and also the lower part of the mesentery of the small bowel.

The rotation of the intestinal loop and the return of the coils to the abdomen take place before the middle of the 3rd month. The condition of parts, later in that month, is shown in Fig. 361. The great bowel, from caecum to colic angle, crosses the abdomen obliquely from

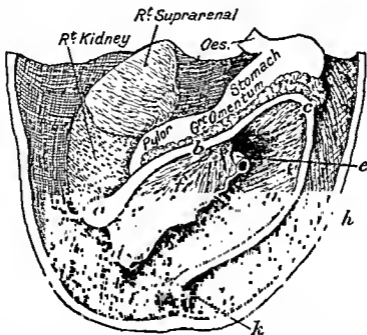


FIG. 361. The Position and Attachments of the Great Bowel late in the 3rd month of development. (After Prof. Frazer.)

a, caecum; b, transverse colon; c, splenic angle; d, ileum; e, duodeno-jejunal junction; f, mesentery; g, meso-colon; h, descending colon; k, rectum

the right iliac crest to the left hypochondrium, where the colic angle is passing towards the spleen. The transverse meso-colon, containing the middle colic artery, is being brought into apposition with that part of the mesogastrium which forms the great omentum (Figs. 361, 364). These two layers adhere; thus the transverse meso-colon is formed by the fusion of a part of the dorsal mesogastrium with the mesentery of the posterior limb of the U-shaped loop (Fig. 336). The rotation has placed

position in front of the right kidney and inferior vena cava. The caecum

demarcated. At first the colic part of the intestinal loop and the caecal process are not of larger calibre than the small intestine, and this continues until the 5th month, when the colon and caecum undergo an enlargement, but the terminal or apical part of the caecum retains its foetal dimensions, and forms the appendix. As in the small bowel, the circular coat appears long before the longitudinal; but whereas the muscle appears first at the proximal end of the small bowel and spreads distally, the muscle of the colon appears first (at the end of the 2nd month) at the rectal end—where the sacral visceral nerves enter—and spreads towards the ileo-caecal junction. The longitudinal coat appears in the 3rd month along the mesenteric border—representing the mesenteric

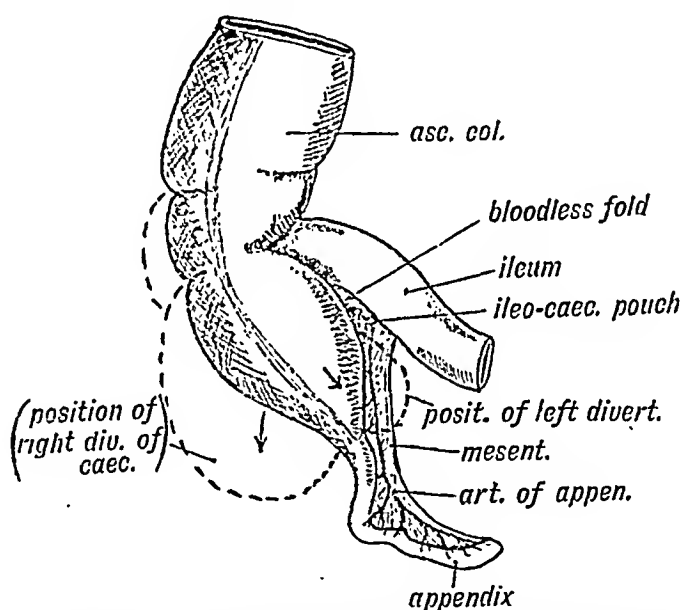


FIG. 360. Diagram of the Apex of the Caecum at the time of Birth and the Diverticula which may be produced later in the Fundus of the Caecum.

taenia; the remaining two are developed in the 4th month. The muscular fibres of the circular coat are arranged as a continuous spiral (Eben Carey) [22]. The evaginations or haustra are distinct in the 7th month of foetal life [23]. Villous processes appear on the mucous membrane in the 4th month and disappear in the 6th. Lymphoid follicles are formed in the mid-colon in the 4th month and, a little later, in the caecum and appendix. The muscular coats of the appendix are developed in the 2nd month [24].

As the superior mesenteric (vitelline) artery descends in the intestinal loop, it gives off three branches to the posterior limb—the middle colic, right colic and ileo-colic arteries (Fig. 356). The mesentery of the U-shaped loop may be divided into two parts, the fate of the two parts being different:

1. The mesentery of the anterior limb, in front of the superior mesenteric artery: forms the *pre-arterial part*. This gives rise to the greater part of the mesentery of the small bowel.

2. The mesentery of the posterior limb, behind the artery: is the *post-arterial part*. It forms the mesentery of the ascending and transverse colon, and also the lower part of the mesentery of the small bowel.

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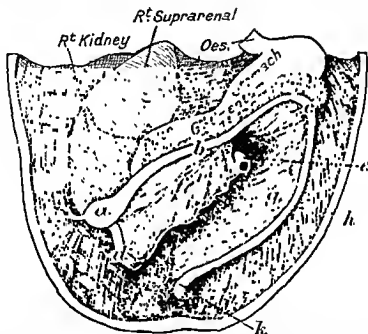


FIG 361. The Position and Attachments of the Great Bowel late in the 3rd month of development (After Prof. Frazer)

a, caecum; b, transverse colon; c, splenic angle; d, ileum; e, duodeno-jejunal junction; f, mesentery; g, meso-colon; h, descending colon; i, rectum

the right iliac crest to the left hypochondrium, where the colic angle is passing towards the spleen. The transverse meso-colon, containing the middle colic artery, is being brought into apposition with that part of the mesogastrium which forms the great omentum (Figs. 361, 364). These two layers adhere; thus the transverse meso-colon is formed by the fusion of a part of the dorsal mesogastrium with the mesentery of the posterior limb of the U-shaped loop (Fig. 336). The rotation has placed the mesentery of the caecum and ascending colon against the duodenum, and at the same time the duodenal loop has become fixed in its permanent position in front of the right kidney and inferior vena cava. The caecum

thus comes to be situated in the majority of foetuses over the right iliac crest and in front of the lower part of the right kidney, near the gall bladder, and there it remains until about the time of birth, when the ascending colon elongates and the caecum thus moves towards the right iliac fossa. In the enlargement of the abdominal space, both before and after birth, the elongation and extension of the lumbar spine must also be taken into consideration. After birth the gall bladder and lower border of the liver ascend, and thus room is made for the ascending colon in the right lumbar region. The hepatic flexure therefore comes into being as the liver recedes [25]. An iliac position of the caecum is a feature which occurs only in animals adapted to the upright posture. Thus the attachment of the ascending meso-colon is effected by secondary adhesions which are formed as the caecum and ascending colon take up their new positions in the right lumbar region. The appendix, during the migration, may be caught behind the colon, thus assuming a *retro-colic position*; it is then lodged and fixed in the ascending meso-colon [26]. The peritoneal adhesions, which are formed in the 4th and 5th months of foetal life, between the transverse meso-colon and great omentum, and especially the adhesions which the ascending colon forms just before and after birth, as the caecum assumes its final position in the iliac fossa, are subject to a great range of variations, and many peritoneal folds and recesses may be formed [27]. The object of all of them is to give a fixation of the viscera to the abdominal wall—a fixation which occurs only in orthograde primates.

The Appendix.—At first, and until the 5th month, the caecal diverticulum is of the same calibre throughout, but from that month onwards, the appendix remains small while the caecum grows, keeping pace in diameter with the colon. At birth the appendix is still the tapered apex of the caecal diverticulum (Fig. 360), but during childhood an outer or an inner sacculation, or both together, arise in the fundus of the caecum and thrust the appendix backwards and to the left into an asymmetrical position [28]. Villi are formed in the mucous coat in the early part of the 4th month; Lieberkühn's glands appear a little later. Lymphoid follicles make their appearance in the 5th month. The villi disappear in the 8th month.

Although a distinctly marked appendix is only seen in man, the anthropoids, lemur, opossum and certain rodents, still a corresponding lymphoid structure is present generally in mammals. The appendix is a lymphoid diverticulum of the caecal apex (R. J. Berry). It must be regarded as a lymphoid structure, and although it can be dispensed with, is not therefore to be regarded as vestigial in nature any more than is the tonsil. In 30% of adults both muscular and mucous coats have undergone a

partial degeneration under modern conditions of diet, and the appendix does tend to become a useless structure.

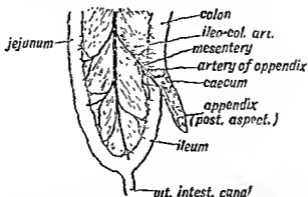


FIG. 362 The Appendix and Pental folds at the end of the 2nd month of Foetal Life. The intestinal loop is viewed on its left aspect, which becomes applied to the dorsal wall of the abdomen

Ileo-caecal Valves.—At the ileo-colic junction, the full development of villi ends. In the higher primates the junction is invaginated within the caecum, the invagination becoming apparent in the human foetus

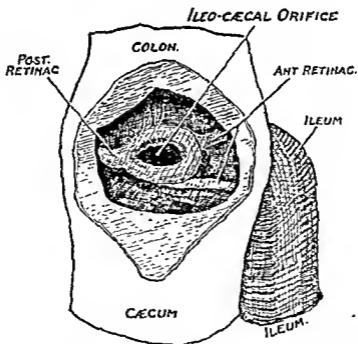


FIG. 361. The Caecum opened to expose the Ileo-caecal Orifice in a Foetus of 8 months. (After Lohm-Epstein.)

of the 3rd month. The ileo-caecal orifice has rounded, continuous lips (Fig. 363). We have already seen how the sphincter of the orifice is developed (p. 417). From the posterior fornix there is developed one

retinaculum or fold—the posterior ileo-colic ; while from the rounded anterior fornix usually two retinacula arise—the upper being the ileo-colic, the lower the ileo-caecal. These are developed in the later months of foetal life [29]. Muscular bands develop in the *retinacula* from the circular musculature of the caecum and represent the *mid-caecal* sphincter of the typical caecum (Fig. 358). The retinacular musculature assists in the emptying and filling of the caecum. To a very slight extent the ileo-colic lips can serve as mechanical valves in the living subject ; they assume a valvular form only when dead and dried.

Ileo-caecal Fossae.—When the caecal diverticulum grows out from the hinder limb of the U-shaped loop it carries with it three folds (see Fig. 364) :

1. The *ileo-colic fold*, a process from the right side of the mesentery

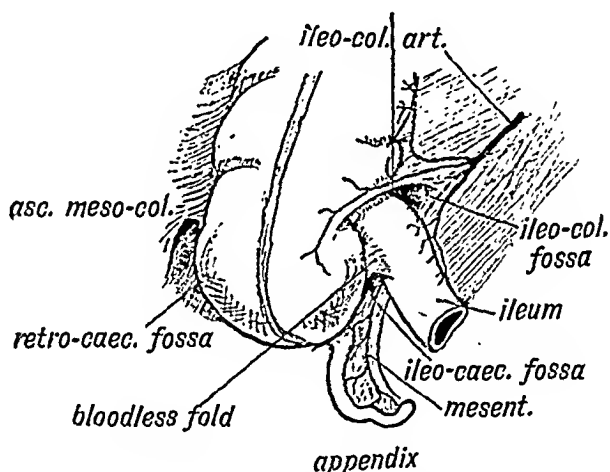


FIG. 364. Peritoneal Fossae in the Ileo-caecal Region.

containing the anterior caecal artery ; in a small proportion of cases this fold forms the mesentery of the appendix [30] ;

2. The *bloodless or ileo-caecal fold*, a process from the wall of the ileum ;

3. The *mesentery of the appendix*, a process from the left side of the mesentery, containing the artery to the appendix (Fig. 362).

These three folds give rise to three *fossae* (Fig. 364) :

1. The *ileo-colic*, between the termination of ileum and ileo-colic fold ;
2. The *ileo-caecal*, between the bloodless fold and mesentery of the appendix ;
3. The *retro-caecal*, between the mesentery of the appendix and commencement of the ascending meso-colon.

The caecum and appendix are made up of bilateral halves ; there are right (anterior caecal fold) and left (mesentery of appendix) mesenteries. In birds the appendix is divided ; it is occasionally double in malformed

human infants [31]. There is no reason to suppose, however, that the appendix was ever a double structure in the stem from which man has descended.

The *duodeno-jejunal fossa* is formed to the left of the duodeno-jejunal flexure after the transverse colon and caecum have become transposed to the right hypochondrium and when the transverse meso-colon has fused with the omental layers of the lesser sac (Fig. 365). The fossa is occupied by the bend of the duodenal-jejunal junction and serves as a bursa for this knuckle of gut. The origin of the fossa is connected with the origin of the traction bands developed at this junction (see p. 409); the inferior mesenteric vein passes in or near the left border of the fossa.

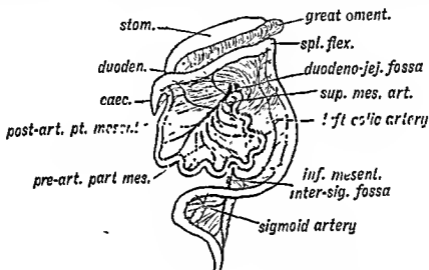


FIG. 365 To show the Rotation of the Intestinal Loop and Formation of the Duodeno-jejunal Fossa

The fossa lies in the axis at which the mesenteric rotation takes place (Fig. 365), and when the plastic nature of the peritoneal tissue is remembered, it is easy to realize how this and other recesses may be formed near the termination of the duodenum.

The mesentery of the small gut is formed out of the primitive mesentery of the U-shaped intestinal loop, chiefly from that part of it (the pre-articular) which lies between the superior mesenteric artery and the anterior limb of the loop (Fig. 356). After the rotation, the aspect of the mesentery which was directed towards the right becomes left and anterior (compare Figs. 350, 365). During the rotatory transposition of the gut the superior mesenteric artery comes to lie in front of the 3rd stage of the duodenum. At first the mesentery of the small intestine is attached in front of the spine near the origin of the superior mesenteric artery (see Figs. 335, 336). Its oblique attachment to the posterior

retinaculum or fold—the posterior ileo-colic ; while from the rounded anterior fornix usually two retinacula arise—the upper being the ileo-colic, the lower the ileo-caecal. These are developed in the later months of foetal life [29]. Muscular bands develop in the *retinacula* from the circular musculature of the caecum and represent the *mid-caecal* sphincter of the typical caecum (Fig. 358). The retinacular musculature assists in the emptying and filling of the caecum. To a very slight extent the ileo-colic lips can serve as mechanical valves in the living subject ; they assume a valvular form only when dead and dried.

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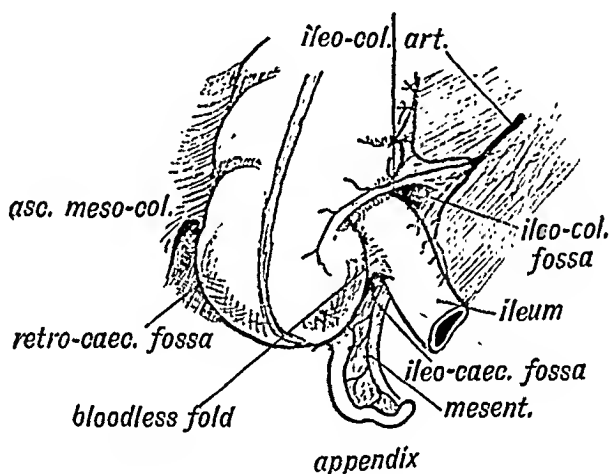


FIG. 364. Peritoneal Fossae in the Ileo-caecal Region.

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The caecum and appendix are made up of bilateral halves ; there are right (anterior caecal fold) and left (mesentery of appendix) mesenteries. In birds the appendix is divided ; it is occasionally double in malformed

[3] Keith, Sir A., *Lancet*, 1910, 2, 362; Guttierrez, R. A., *Morfogenesis Peritoneo-intestinal*, Buenos Aires, 1929; Baron, M. A., *Amer. Jour. Anat.*, 1942, 69, 439 (development of subperitoneal tissue).

[4] Reid, D. G., *Jour. Anat.*, in volumes from 1911 to 1915.

[5] For description of muscle of Treitz, see references to Low and to Crymble, in note [1].

[6] Papez, J. W., *Anat. Rec.*, 1932, 54, 197.

[7] For accounts of the rotation and fixation of the alimentary canal in foetus, see Frazer, J. E., *Manual of Embryology*, 1940; Bardeen, C. R., *Amer. Jour. Anat.*, 1914, 16, 427; Ginglinger, A., *Archiv. d'Anat.*, 1935, 20, 283 (retraction process in pig foetus); Aasar, Y. H., *Jour. Anat.*, 1938, 72, 579.

[8] For an account of the yolk-sac and of its vestiges, see Jordan, H. E., *Anat. Anz.*, 1907, 31, 291; 1910, 37, 56. The yolk-sac of the guinea-pig absorbs vital dyes with avidity (Nicol, T., *Jour. Anat.*, 1932, 66, 181); for vestiges, see Keith, Sir A., *Brit. Med. Jour.*, 1910, 1, 301; Zimmermann, A. A., *Anat. Rec.*, 1934, 58, 245 (Meckel's diverticulum in foetus).

[9] Nicholson, G. W., *Jour. Path. Bact.*, 1922, 25, 201.

[10] Lewis, F. T., *Anat. Rec.*, 1934, 58, 25 (suppl.); Patzelt, V., and Pernkopf, E., see references in note [1], Chapter XX. Pei-Lin Li, *Jour. Anat.*, 1940, 74, 348 (for development of Auerbach's plexus); for differentiation of coats under experimental conditions, see Waterman, A. J., *Anat. Rec.*, 1938, 70, 107 (suppl.).

[11] Lewis and Thyng, *Amer. Jour. Anat.*, 1908, 7, 505; Evans, Arthur, *Brit. Jour. Surg.*, 1929, 17, 34; MacAuley, H. F., *ibid.*, 1923, 11, 122; Buxton, St. J. D., *Jour. Anat.*, 1924, 58, 85; Grant, J. C. B., *Canadian Med. Ass. Jour.*, 1935, 33, 258 (of duodenum); Walmsley, T., *Jour. Anat.*, 1930, 64, 47 (of appendix) Wierda, J. L., *Anat. Rec.*, 1941, 79, 109 (hernial diverticula of duodenum).

[12] Evans, Arthur, see reference in note [11].

[13] McMurrieh and Tindall, *Anat. Rec.*, 1928, 39, 325; Edwards, H., *Brit. Jour. Surg.*, 1927, 17, 7.

[14] Johnson, F. P., *Amer. Jour. Anat.*, 1913, 14, 187.

[15] Wakeley, C. P. G., *Jour. Anat.*, 1930, 64, 527; Halpert, B., *Bull. Johns Hopkins Hosp.*, 1926, 38, 409.

[16] Wakeley, C. P. G., *Jour. Anat.*, 1923, 57, 216; Keith, Sir A., *Brit. Med. Jour.*, 1910, 1, 301; Odgers, P. N. B., *Brit. Jour. Surg.*, 1930, 17, 592.

[17] See references to Low and to Crymble, note [1].

[18] Tönbury, G., *Zeitsch. Anat. Entwickl.*, 1933, 100, 753; Schapschal, J., *ibid.*, 1934, 102, 44; Groth, W., *ibid.*, 1933, 101, 234; Reider, N., *Proc. Zool. Soc. Lond.*, 1936, p. 433 (pelvic colon in primates); Kantor, J. L., *Radiology*, 1934, 23, 651.

[19] Keith, Sir A., *Proc. Anat. Soc.*, November, 1903; Johnston, T. B., *Jour. Anat.*, 1920, 54, 67; Rutberford, A. H., *ibid.*, 1926, 80, 411; Hill and Rewell, *Trans. Zool. Soc. Lond.*, 1948, 26, 199. (The caecum of primates.)

[20] The morphology of the ileo-caecal tract is dealt with by: Lorin-Epstein, M. J., *Zeitsch. Anat. Entwickl.*, 1932, 97, 68; Weissberg, H., *ibid.*, 1931, 107, 738; Hunter, R. H., *Jour. Anat.*, 1934, 68, 264.

[21] Beattie, J., *Jour. Anat.*, 1924, 59, 56; Hunter, R. H., *Ulster Med. Jour.*, January, 1936.

[22] Carey, E. J., *Anat. Rec.*, 1921, 21, 189; Laneback, P. E., *Contrib. Emb.*, 1920, 11, 33 (development of taenia); Hunter, R. H., *Jour. Anat.*, 1928, 62, 297.

abdominal wall, from the duodenum to the right iliac fossa, is effected by secondary adhesions which are formed after the rotation of the gut and during the 4th and 5th months, and this extensive attachment is found only in animals adapted to the upright posture. The last part of the mesentery to become adherent to the posterior wall of the abdomen is the angular area between the ileum and ascending colon. Not unfrequently this part remains free, and it is then possible for a *volvulus* to form by a rotation of the ileo-colic loop.

By the rotation of the U-shaped loop, the small intestine becomes confined in a bursa or peritoneal compartment formed by the mesentery of the large bowel (Fig. 365).

Abnormal Fixation of the Mesentery.—The rotation of the bowel is subject to three forms of disturbance, giving rise to three varieties in the fixation of the mesentery, which are of importance to medical men [32]: (i) The bowel may undergo its normal rotation, but the process of adhesion may fail; the bowel is thus suspended by a free fan-shaped mesentery. During life it may become twisted round its stalk, formed by the superior mesenteric artery, and thus give rise to obstruction of the bowel (complete *volvulus*). (ii) It may not undergo a rotation; the caecum then lies on the left side of the abdomen, and the colon—ascending and descending—are situated behind and to the left of the small bowel. (iii) The rotation may occur in a direction opposite to the normal—the duodenum and mesentery coming to lie in front of the transverse colon in place of being situated behind it. Several cases of this nature have been recorded of late by surgeons and anatomists.

Meconium.—At birth, the great intestine and the lower part of the ileum are distended by meconium, a black, semi-fluid substance secreted by the liver and mucous membrane of the bowel. Prof. Low found that the meconium reaches the ileo-colic junction in the 4th month, the rectum in the 5th. The meconium passes quickly along the jejunum. By the 3rd or 4th day after birth all the meconium has been passed, a fact which may be utilized to prove that a child had lived for a certain time after birth. There is evidence that the foetus swallows and absorbs the amniotic fluid in which it is immersed [33]. In this way peristaltic activity on the part of the intestine is stimulated. Peristalsis begins late in the 3rd month of development.

NOTES AND REFERENCES

[1] For accounts of the fixation of the duodenum, see Frazer, J. E., *Jour. Anat.*, 1927, 61, 356; Hunter, R. H., *ibid.*, 1927, 61, 206; Low, A., *ibid.*, 1908, 42, 93; Crymble, P. T., *Brit. Med. Jour.*, 1910, 2, 1156.

[2] Tönbury, G., *Zeitsch. Anat. Entwickl.*, 1937, 106, 251; Bucher, O., *ibid.*, 1937, 107, 388 (types of duodenal loop).

CHAPTER XXII

CIRCULATORY SYSTEM

Early Stages in the Evolution of the Heart.—In the larval form of the lamprey, *Ammocoetes*, is represented the most primitive form of heart in vertebrate animals. Even in this early type the heart consists of four chambers (Fig. 366) : (i) Sinus venosus, receiving the portal blood from the liver ; (ii) auricle ; (iii) ventricle ; (iv) bulbus cordis, from which the primitive ventral aorta passes out to distribute the blood in the branchial chamber. The primitive heart is thus a respiratory pump that

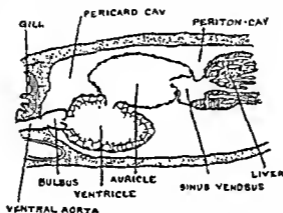


FIG 366 The Heart of *Ammocoetes* seen in a Median Section. (After Vialleton)

forces the portal blood through a branchial system. It is clear, then, that the early evolutionary stages of the heart must be sought for amongst invertebrate forms, but these stages are as yet unknown. When the heart appears in the human embryo, towards the end of the 3rd week, it is double—consisting of right and left plexiform blood spaces. We therefore suppose that originally there were right and left hearts, which arose as modifications of the vessels which convey the blood from the alimentary to the respiratory systems. In Fig. 367 the left side of such a primitive circulation is represented. The left heart forces the blood along a primitive dorsal aorta to the capillary system of the archenteron. An afferent (primitive portal) vessel conveys the blood back to the heart. When the head and tail folds are produced in the embryonic plate at the beginning of the 4th week (see Fig. 367), the right and left cardiac tubes are thrust under the fore-gut, where they speedily become fused into a median heart [1]. In its origin the heart is thus made up of symmetrical

[23] Carey, E. J., *Anat. Rec.*, 1920, 18, 224; Thaysen, T., *Anat. Hefte*, 1916, 54, 321.

[24] Horowitz, E., *Zeitsch. Anat. Entwickl.*, 1933, 101, 679; Patzelt, V., reference in note [1], Chapter XX.

[25] The descent of the caecum and appendix has been discussed and denied by Prof. Frazer (*Manual of Human Embryology*, 1940) and by Dr. R. H. Hunter (*Jour. Anat.*, 1928, 62, 297). My own observations have led me to an opposite conclusion.

[26] For an account of the variations in the position of the appendix, see Wakeley, C. P. G., *Jour. Anat.*, 1933, 67, 277; Collins, D. C., *Ann. Surg.*, 1932, 96, 1044.

[27] Reid, D. G., see under note [4].

[28] Parsons, F. G., *Jour. Anat.*, 1908, 42, 30; Lorin-Epstein, see note [20].

[29] See references to Lorin-Epstein in note [20], and to Rutherford in note [19].

[30] Smith, G. M., *Anat. Rec.*, 1911, 5, 549; Forster, A., *Anat. Hefte*, 1918, 56, 5.

[31] Wood-Jones, F., *Jour. Anat.*, 1912, 46, 193; Cave, A. J. E., *ibid.*, 1936, 70, 283; Greig, D. M., *Edin. Med. Jour.*, 1934, 41, 277; Clavel and Colson, *Ann. d'Anat., Path.*, 1934, 11, 157.

[32] Dott, N. M., *Brit. Jour. Surg.*, 1923, 11, 251; Aasar, Y. H., *Jour. Anat.*, 1938, 72, 579; Papez, J. W., *Anat. Rec.*, 1932, 54, 179.

[33] *Year Book of the Carnegie Institution*, Washington, 1943, 42, 111.

Ammocoetes—but with the origin of a pulmonary system a series of most remarkable changes occur. The pulmonary system in the human embryo takes on its definite form during the 2nd month; at the same time the heart is undergoing a series of changes, which converts it into a double pump, one for the lungs, another for the body. We know that these evolutionary changes occurred slowly, for even in *amphibia* the heart has only reached that point in evolution where a single ventricle has to serve both the respiratory and systemic circulations. The evolution of a pulmonary system also led to a series of changes in the arrangements of veins. Amongst the most remarkable of these is the formation of a new passage by which the blood of the abdomen can pass direct to the heart—the inferior vena cava. In the human embryo of the 5th week

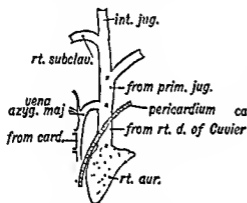


FIG. 368.

FIG. 368. The Superior Vena Cava of the Adult

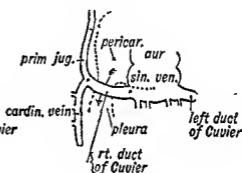


FIG. 369

FIG. 369 The Embryonic Venous Trunks out of which the Superior Vena Cava is formed. The arrow is in the communication between the pericardial and pleuro-peritoneal cavities (See Fig. 370)

the heart and great veins are arranged as in a fish; in the 7th week they take on the definite mammalian form.

Fixation of the Heart.—At the beginning of the 4th week (Fig. 327) the heart lies free within the pericardium, with its two extremities fixed to the wall of that cavity (Figs. 388, 392). Its anterior or arterial extremity perforates the dorsal wall of the pericardium to give off the aortic arches in the floor of the pharynx (Fig. 293). The venous or posterior end is fixed to the septum transversum, the embryonic partition, which is formed between the pericardial and peritoneal cavities (Fig. 327). The fate of the aortic arches, which convey the blood from the ventral to the dorsal aorta, has been already traced (p. 357). We now propose, before surveying the complicated changes that ensue in the heart itself, to trace the evolution of those great venous channels which convey the blood to the heart—the venae cavae.

The superior vena cava arises from the following foetal vessels (Figs. 368, 369):

halves derived from the corresponding sides of the body—halves which come into apposition and unite to form a single heart, a remarkable example of developmental surgery. The parts that form the ventricles are already pulsating as union takes place. When formed, the heart is suspended within the anterior part of the coelomic space—which becomes the cavity of the pericardium. In *Ammocoetes* the pericardial and peritoneal cavities are continuous (Fig. 366).

✧ **Angioblastic Tissue.**—That the cardiac tube has arisen by the modification of a blood-vessel is apparent by the way it commences to form in the human embryo. Late in the 3rd week certain cells become grouped under the fore-gut to form the lining membrane of the heart. At the

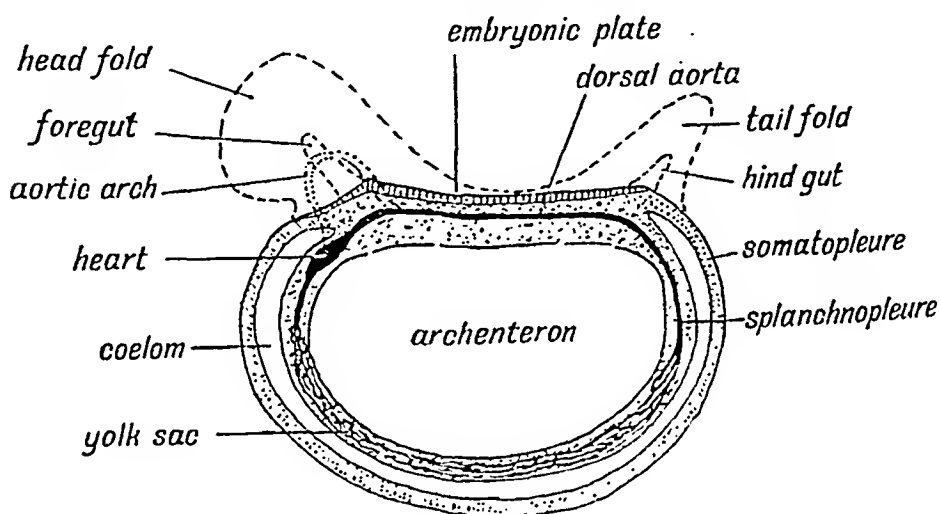


FIG. 367. Diagram showing the Relationship of the Heart to the Archenteron of the Developing Ovum. The outgrowth of the head fold is indicated carrying a process (fore-gut) of the archenteron and also the aorta and heart. The outgrowth of the tail fold and hind-gut is also shown. (After Prof. A. Robinson.)

same date similar cells in the chorionic villi, in the wall of the yolk sac and along the tracks of the future aortae, are grouping themselves in an identical manner to form the lumina of blood channels. The mesodermal cells that have this vessel-forming power pervade the whole embryonic mass and are known as angioblasts. One group of angioblasts unites with neighbouring groups, thus forming a network. Further, angioblasts not only form the lining cells and lumina of blood-vessels but also produce the blood cells and plasma that fill them. A "blood island" is a group of angioblasts surrounding a brood of nucleated red corpuscles. When neighbouring islands unite the essential part of the circulatory system has come into existence. The lining of the heart arises in the same manner as a simple capillary.

Later Stages in the Evolution of the Heart.—So long as the heart is merely a pump for the gills, it retains the simple structure seen in

Ammocoetes—but with the origin of a pulmonary system a series of most remarkable changes occur. The pulmonary system in the human embryo takes on its *definite form during the 2nd month*; at the same time the heart is undergoing a series of changes, which converts it into a double pump, one for the lungs, another for the body. We know that these evolutionary changes occurred slowly, for even in amphibia the heart has only reached that point in evolution where a single ventricle has to serve both the respiratory and systemic circulations. The evolution of a pulmonary system also led to a series of changes in the arrangements of veins. Amongst the most remarkable of these is the formation of a new passage by which the blood of the abdomen can pass direct to the heart—the inferior vena cava. In the human embryo of the 5th week

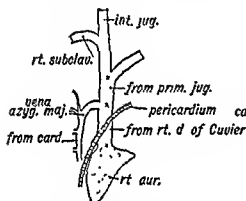


FIG. 368.

FIG. 368. The Superior Vena Cava of the Adult

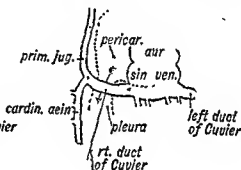


FIG. 369.

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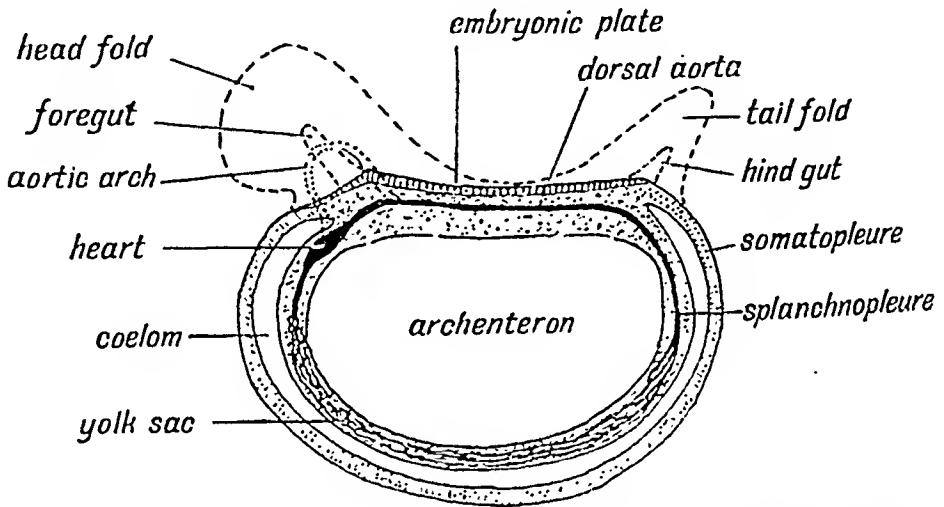


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Later Stages in the Evolution of the Heart.—So long as the heart is merely a pump for the gills, it retains the simple structure seen in

cavities. Thus the exit from the pericardial cavity to the pleural passage is surrounded on each side by a great venous channel—the duct of Cuvier; hence the exit is sometimes named the *iter venosum* or *pericardio-pleural* passage. Ultimately, by the end of the 6th week, the anterior part of the coelom, bounded posteriorly by the ducts of Cuvier and septum transversum, is cut off from the rest; the part so cut off forms the pericardium. In the 4th week the dorsal margin of the septum transversum is situated opposite to the 2nd cervical segment; by the end of the 6th week, the embryo being then about 10 mm. long, it has shifted backwards so as to lie on a level with the 3rd thoracic segment, in this way bringing the duct of Cuvier into an oblique position (Fig. 388). Thus the ducts of Cuvier are instrumental in separating the pericardial

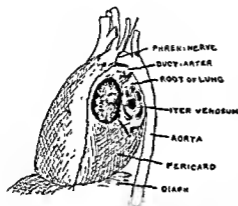


FIG. 371.

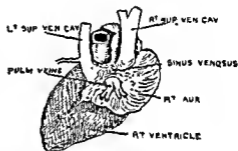


FIG. 372.

FIG. 371. Heart of a Child, showing an Abnormal Aperture in the Pericardium in front of the root of the Left Lung, representing a patent *Iter Venosum* or *Pericardio-pleural* passage of the Embryo. The left auricle is seen within the aperture.

FIG. 372. Abnormal Heart of a Child seen from behind, showing Persistence of the Left Duct of Cuvier, absence of the Inferior Vena Cava, and with the Pulmonary Veins terminating in the Sinus Venosus. A similar condition is seen in certain fishes.

from the pleural cavity. If the primitive pleuropericardial communication (*iter venosum* of Lockwood) persists between them, it occurs as a foramen in the pericardium behind the part of the superior vena cava derived from the duct of Cuvier [2]. On the left side the duct of Cuvier atrophies, and the *iter venosum*, if it persists, is then represented by an aperture in the pericardium in front of the root of the left lung (Fig. 371). The ducts of Cuvier, and the folds of the somatopleure in which they lie, are eventually separated from the body-wall and buried deep in the thorax by the development of the lungs and pleurae.

Vestigial Fold and Oblique Vein of Marshall.—In the human embryo during the 4th week and for two weeks afterwards there is a right and left duct of Cuvier and corresponding cardinal veins (Fig. 374). A left superior vena cava is present and persists (Fig. 372). The vestigial

cavities. Thus the exit from the pericardial cavity to the pleural passage is surrounded on each side by a great venous channel—the duct of Cuvier; hence the exit is sometimes named the *iter venosum* or *pericardio-pleural* passage. Ultimately, by the end of the 6th week, the anterior part of the coelom, bounded posteriorly by the ducts of Cuvier and septum transversum, is cut off from the rest; the part so cut off forms the pericardium. In the 4th week the dorsal margin of the septum transversum is situated opposite to the 2nd cervical segment; by the end of the 6th week, the embryo being then about 10 mm. long, it has shifted backwards so as to lie on a level with the 3rd thoracic segment, in this way bringing the duct of Cuvier into an oblique position (Fig. 388). Thus the ducts of Cuvier are instrumental in separating the pericardial

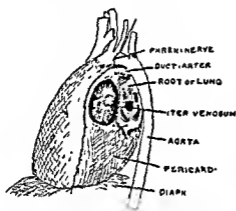


FIG. 371.

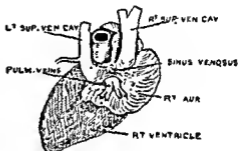


FIG. 372

FIG 371. Heart of a Child, showing an Abnormal Aperture in the Pericardium in front of the root of the Left Lung, representing a patent Iter Venosum or Pericardio-pleural passage of the Embryo. The left auricle is seen within the aperture.

FIG 372. Abnormal Heart of a Child seen from behind, showing Persistence of the Left Duct of Cuvier, absence of the Inferior Vena Cava, and with the Pulmonary Veins terminating in the Sinus Venosus. A similar condition is seen in certain fishes.

from the pleural cavity. If the primitive pleuropericardial communication (*iter venosum* of Lockwood) persists between them, it occurs as a foramen in the pericardium behind the part of the superior vena cava derived from the duct of Cuvier [2]. On the left side the duct of Cuvier atrophies, and the *iter venosum*, if it persists, is then represented by an aperture in the pericardium in front of the root of the left lung (Fig. 371). The ducts of Cuvier, and the folds of the somatopleure in which they lie, are eventually separated from the body-wall and buried deep in the thorax by the development of the lungs and pleurae.

Vestigial Fold and Oblique Vein of Marshall.—In the human embryo during the 4th week and for two weeks afterwards there is a right and left duct of Cuvier and corresponding cardinal veins (Fig. 374). A left superior vena cava is present and may persist (Fig. 372). The vestigial

fold and oblique vein of Marshall (Fig. 373) are all that usually remain of the left superior vena cava. The right superior vena cava, within the pericardium, passes in front of the right pulmonary vessels, and is bound to them by a mesentery or fold of serous pericardium; the left has a similar relationship (Fig. 373); when it disappears the pericardial reflection remains in front of the left pulmonary vessels as the vestigial fold. The intra-pericardial part of the left vena cava or duct of Cuvier becomes the oblique vein: it turns round the left auricle to terminate in the left horn of the sinus venosus (coronary sinus). The extra-pericardial part of the left duct of Cuvier joins the superior intercostal

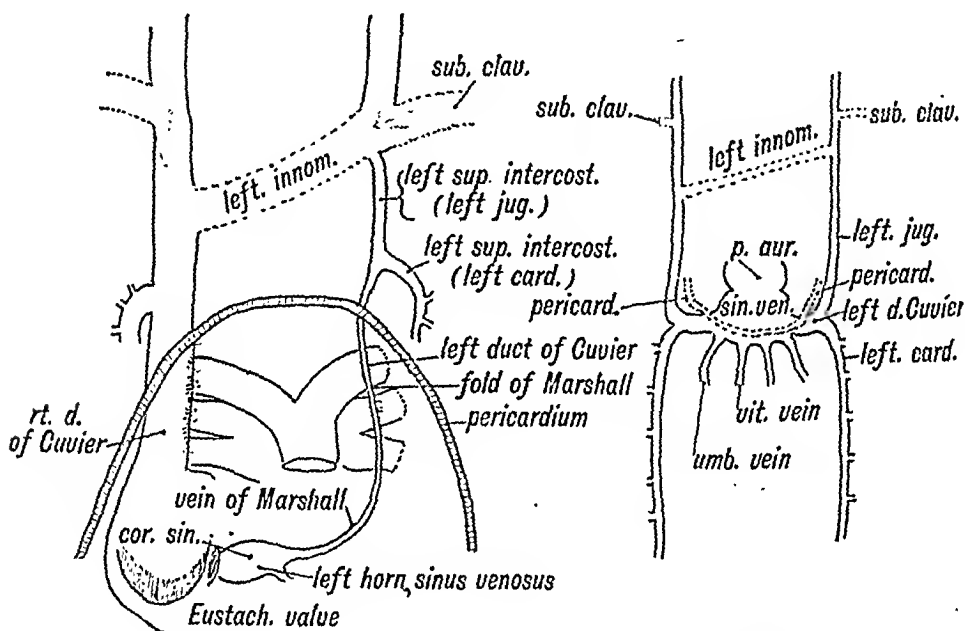


FIG. 373.

FIG. 374.

FIG. 373. The Remnants of the Left Superior Vena Cava, derived from the Structures shown in Fig. 374.

FIG. 374. Diagram of the Sinus Venosus and Ducts of Cuvier of the Human Embryo in the 4th week.

vein (Fig. 373). Both right and left superior venae cavae persist in some lower mammals, and occasionally this is also the case in man [3]. The left superior vena cava begins to atrophy when the common auricular chamber is divided into a right and left compartment in the 6th and 7th weeks.

The *left superior intercostal vein* represents the following embryonic vessels (see Fig. 373): (a) anterior part of the left posterior cardinal vein; (b) the extra-pericardial part of the left duct of Cuvier; (c) the terminal part of the left primitive jugular vein.

The *left innominate vein* opens up as a channel of communication between the two primitive jugular veins, the left superior vena cava undergoing, at the same time, a process of atrophy (Fig. 373).

The *subclavian vein* appears in the 5th week with the outgrowth of the arm bud. It joins an intersegmental vein (the 7th cervical), which at first ends in the posterior cardinal. As the neck becomes differentiated in the 2nd month and the heart moves backwards, the termination of the subclavian vein comes to open into the primitive jugular.

Each *primitive jugular* (anterior cardinal) vein commences within

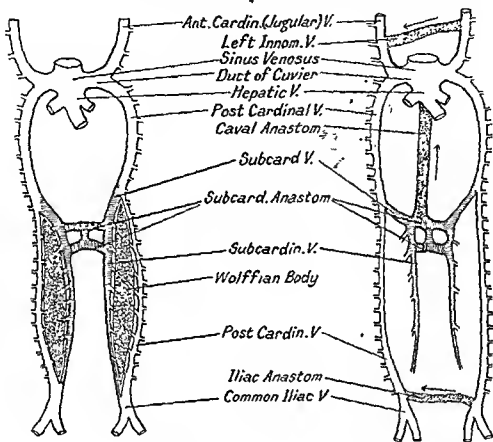


FIG. 375.

FIG. 376.

FIG. 375. Posterior and Subcardinal Veins (shaded)—a stage reached in the 5th week of development

FIG. 376. First Stage in the Evolution of the Inferior Vena Cava, and of Anastomoses between Anterior Cardinals (left innominate vein) and lower end of Posterior Cardinals by iliac anastomosis (left common iliac vein).

the head—as the primitive head vein (see p. 200). The head vein receives tributaries from the fore-, mid- and hind-brains, and makes its exit by the jugular foramen, where it becomes the jugular.

Succession of Abdominal Veins.—The arrangement of veins seen in the human abdomen has a long history. In the developing human embryo there is a succession of three systems of veins [4]. In the 5th week of development the two posterior cardinal veins drain the hinder part of the body (Fig. 375). They commence at the base of the sacrum

by the union of tributaries from the right and left leg buds and from the sacral segments and pass forwards on the dorsal side of the developing Wolffian Bodies (Mesonephroi). The cardinals as they proceed forwards receive tributaries from between each pair of segments (becoming lumbar and intercostal veins) and end by joining the anterior cardinal (primitive jugulars) to form the two ducts of Cuvier. Even at this early stage a change in the venous circulation is being introduced. As in the permanent condition of amphibia, part of the blood from the hinder end of the body passes through the Wolffian bodies before being returned to the heart. The veins that collect the blood from the bodies are known as the *subcardinals*; they join the posterior cardinals (Fig. 375). In the 6th week an important modification is introduced (Fig. 376). A communication opens up between the terminal part of the hepatic vein and the right subcardinal vein. In this way, not only the blood from the Wolffian bodies but also from the hind limbs and hinder part of the body is returned direct to the heart.

After the establishment of this short route to the heart the next change is introduced. This consists of the disappearance of the greater part of both posterior cardinal veins and their replacement by new channels, which are opened up for the return of the blood carried in the intersegmental veins (lumbar and intercostal veins). These new longitudinal channels—known as the *supracardinal veins*—lie on each side of the aorta in front of the vertebrae. Behind they communicate with the sources of origin of the posterior cardinals—the future common iliac veins (Fig. 377); in front they turn outwards to join the terminal parts of the posterior cardinal veins, which persist.

In the *inferior vena cava* are preserved part of all three systems (Fig. 378). The part behind the liver represents the new communication; the part immediately above the renal veins is made up from the right subcardinal. The part below the kidneys is made up mainly from the right supracardinal, but there are also two other elements—(i) an upper, which represents a communication between the right supracardinal and right subcardinal (Fig. 377), and (ii) a lower, the part of the inferior cava lying behind the right common iliac artery, which represents the hinder part of the posterior cardinal system. The renal, spermatic and supra-renal veins, originally ending in the subcardinal veins, now terminate in the inferior vena cava and left renal.

The *azygos veins* arise from the supracardinal system—all save the terminal part of the right azygos vein, a survival from the right posterior cardinal (Fig. 378), and the left superior intercostal, which preserves part of left posterior cardinal. Cross communications open up between the left and right supracardinals. It is by the preservation of one of the

cross communications that the left hemi-azygos obtains access to the vena azygos major (Fig. 378). The left common iliac vein represents a cross communication—not between the hinder ends of the supracardinals but between the posterior cardinals.

Although the parts of the three systems of veins which are preserved to form the superior vena cava and azygos veins are those which have just been mentioned, yet it is not uncommon for other elements to persist.

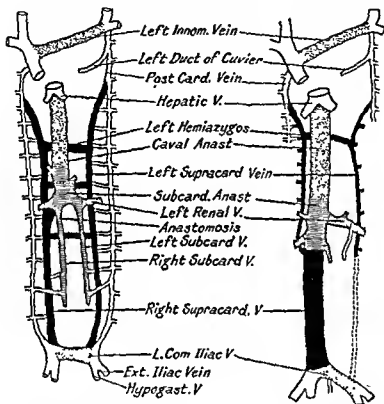


FIG 377

FIG 378.

FIG 377. A conspectus of the Three Systems of Veins (Cardinal, Subcardinal, Supracardinal) that appear in succession during the 2nd month of human development. Each system is indicated by a form of shading. (After R. J. Gladstone.)

FIG 378. The origin of the Inferior Vena Cava and of the Azygos Veins from the Triple Venous System of the Embryo.

—thus giving rise to the numerous abnormalities of the abdominal veins with which anatomists and surgeons are only too familiar. One of the commonest of these abnormalities is a duplication of the infra-renal part of the inferior vena cava [5].

The portal vein is formed out of the terminal parts of the two vitelline veins. They end in the posterior chamber of the tubular heart of the embryo—the sinus venosus. The vitelline veins, right and left, arise from ramifications on the yolk sac and pass in the ventral mesentery

of the fore-gut to the sinus venosus (Fig. 380). The nutriment within the yolk sac is thus carried to the heart and distributed by the heart to the tissues of the embryo and yolk sac. With the differentiation of the gut from the roof of the yolk sac, the left vitelline vein becomes separated from the mesentery as a cord (Fig. 353), the superior mesenteric being formed in the mesentery of the developing mid-gut. Thus while the terminal parts of the vitelline veins lie in the ventral mesentery (gastro-hepatic omentum) of the fore-gut, the three tributaries of the portal vein—the splenic vein from the fore-gut, the inferior mesenteric from the

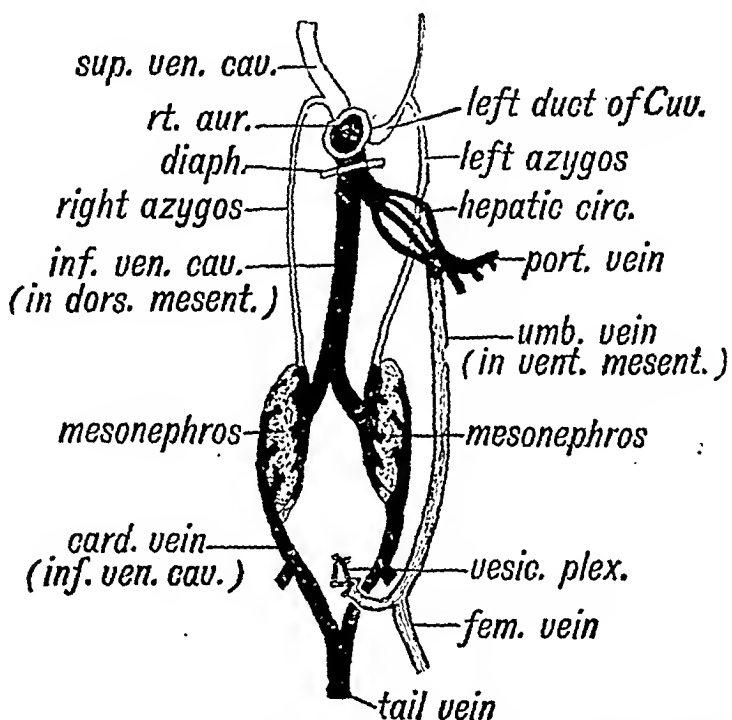


FIG. 379. The arrangement of the Cardinal, Umbilical and Inferior Caval Veins in Lower Vertebrates. The venous blood from the posterior part of the body passes through either the renal or hepatic circulations before reaching the heart. (After Hoesstetter.)

hind-gut, and the superior mesenteric from the mid-gut (Fig. 380)—lie in the dorsal mesentery. They are developed as tributaries of the vitelline veins, for we have already seen that the veins of the yolk sac may persist as a cord which joins the superior mesenteric vein below the pancreas (see Fig. 353). The duodenum forms a loop between the vitelline veins (Fig. 381), and hence on either side of the 1st and 3rd stages of the duodenum the vitelline veins remain separate, while in front, between and behind these stages, they are united by proximal, middle and distal junctions (see Fig. 381).

The portal sinus in the transverse fissure of the liver is formed out of the proximal junction of the right and left vitelline veins in the ventral

mesentery (Figs. 381, 330); the part of the portal vein in the gastro-hepatic omentum (ventral mesentery), and behind the 1st stage of the duodenum, is formed from the right vitelline vein; the corresponding part of the left vein disappears; the commencement of the portal vein—in the neck of the pancreas—represents the middle junction of the two vitelline veins (Fig. 381); the terminal part of the superior mesenteric vein, which in the adult lies in front of the 3rd stage of the duodenum, represents a part of the left vitelline vein—the corresponding part of the right disappears (Fig. 381). To understand the transmutation which

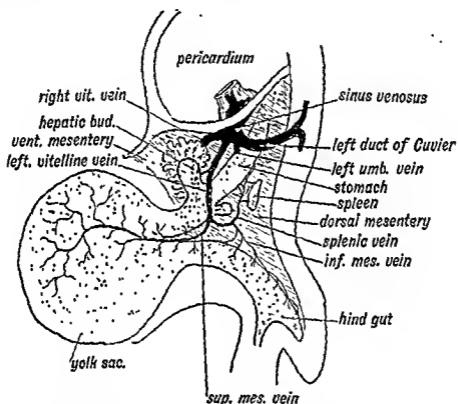


FIG. 330 The Left Vitelline Vein of a Human Embryo of the 5th week.

leads to the formation of the portal vein, it must be remembered (i) that the duodenum forms at first a free loop, the right surface of which afterwards becomes applied to the posterior wall of the abdomen; (ii) the pancreas is developed in its dorsal mesentery; (iii) the ventral mesentery, in which the liver is developed, is attached to the anterior part of the loop (Fig. 380).

Hepatic veins are formed out of the terminal parts of the vitelline veins, but chiefly out of the right, for as we have seen (p. 386), the left ceases to open into the sinus venosus. These veins end at first in the sinus venosus (Figs. 330, 331). The liver is developed between and around

their terminal parts (see p. 385). Thus it comes about that the vitelline veins are transformed into the veins of the portal and hepatic circulation. All the foetal and placental venous blood is at first poured through the liver.

The *ductus venosus* is a new channel formed in the 5th week between the portal sinus and the terminal part of the right vitelline vein, whereby the greater part of the placental blood is short-circuited to the sinus venosus without passing through the liver. After birth, when a short circuit is no longer required between the placental circulation and heart,

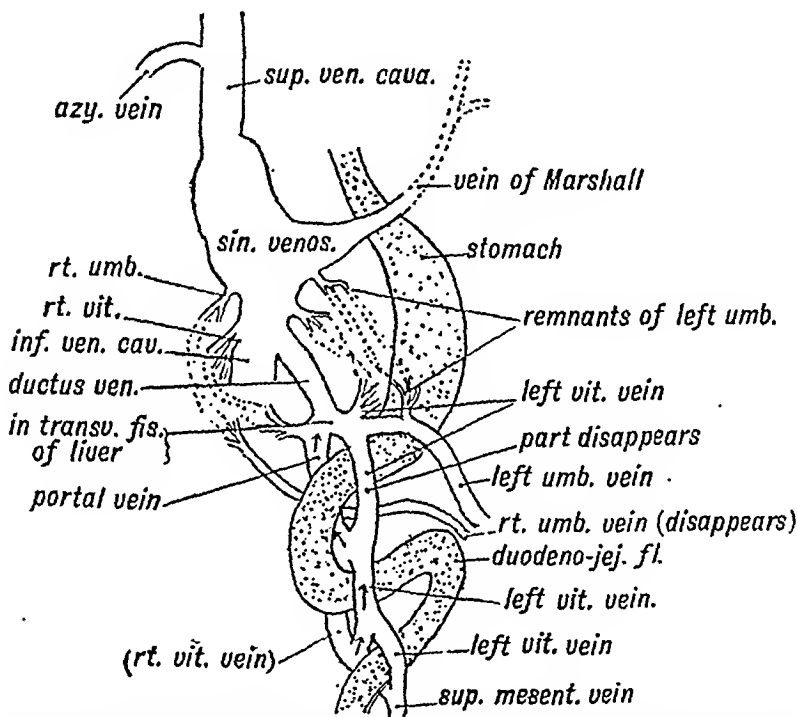


FIG. 381. Diagram showing the formation of the Ductus Venosus, and the fate of the Umbilical and Vitelline Veins. The arrows show the parts of the vitelline veins that become the portal vein.

it becomes reduced to a fibrous cord [6]. It occupies the posterior part of the longitudinal fissure of the liver and lies within the hepatic attachment of the gastro-hepatic omentum (Fig. 382).

Umbilical Veins.—The umbilical vein at birth consists of two parts : (i) a part within the umbilical cord ; (ii) another within the body, enclosed in the falciform ligament and anterior half of the longitudinal fissure of the liver. It joins there the ductus venosus and portal sinus (Fig. 382). The arrangement of the umbilical veins in a human embryo of the 4th week is shown in Fig. 29, and of the 5th week in Fig. 383. The vessel from which the umbilical veins have been evolved—the lateral vein of lower vertebrates—is illustrated in Figs. 31 and 379. In the body-stalk the umbilical veins have already fused (Fig. 299) but in the

body-wall and ventral mesentery, in which they pass to reach the sinus venosus, they remain separate. With the differentiation and closure of the umbilicus, the part of the body-wall in which the umbilical veins are situated grows in length and in thickness to form the umbilical cord. The intra-embryonic parts then lie within the ventral mesentery of the fore-gut, lateral and ventral to the vitelline veins. By the umbilical veins the blood is returned from the placenta to the heart. In nearly all vertebrate embryos the vitelline veins are the first of all the vessels of the body to be developed, but in the higher primates, including man, this appears not to be the case. We have seen (p. 40) that by the 16th day vascular formation has commenced in the chorion while there is as

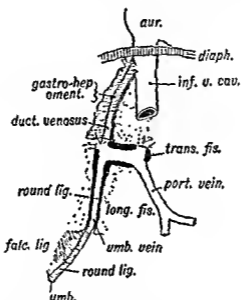


FIG. 332 Diagram of the Remnants of the Umbilical Vein in the Adult—as seen on the dorso-caudal surface of the liver.

yet no sign of the vitelline veins or of the heart. We have noted too (Chapter II) that the higher primates are remarkable for their precocious development of the chorion; this early differentiation of the chorion is attended by an equally early formation of the umbilical vessels, which return the blood from the chorion to the heart.

The outgrowth of the liver-bud within the ventral mesentery breaks up not only the vitelline veins but also the umbilical at their junction with the sinus venosus (Figs. 330, 331). The intra-embryonic part of the right umbilical vein atrophies, while the left enlarges. With the terminal parts of the vitelline veins the opposite is the case. Thus the chorionic blood as well as the vitelline comes to be poured into the liver. The termination of the left umbilical vein is gradually transferred during the 6th and 7th weeks from the sinus venosus to the portal sinus (p. 487)

The left umbilical vein thus comes into communication with the ductus venosus (see Figs. 381, 382).

The Heart as a Placental Pump.—Having thus traced the origin of the great veins which conduct the blood to the heart, we now turn to the development of this organ. In the 4th and 5th weeks the umbilical veins are fully established (Fig. 383) and the heart is receiving the major part of its blood from the chorion, and its chief task is to serve as the pump of that organ. Hence the large size of the heart and pericardium when compared with the actual dimensions of the embryo itself—or the

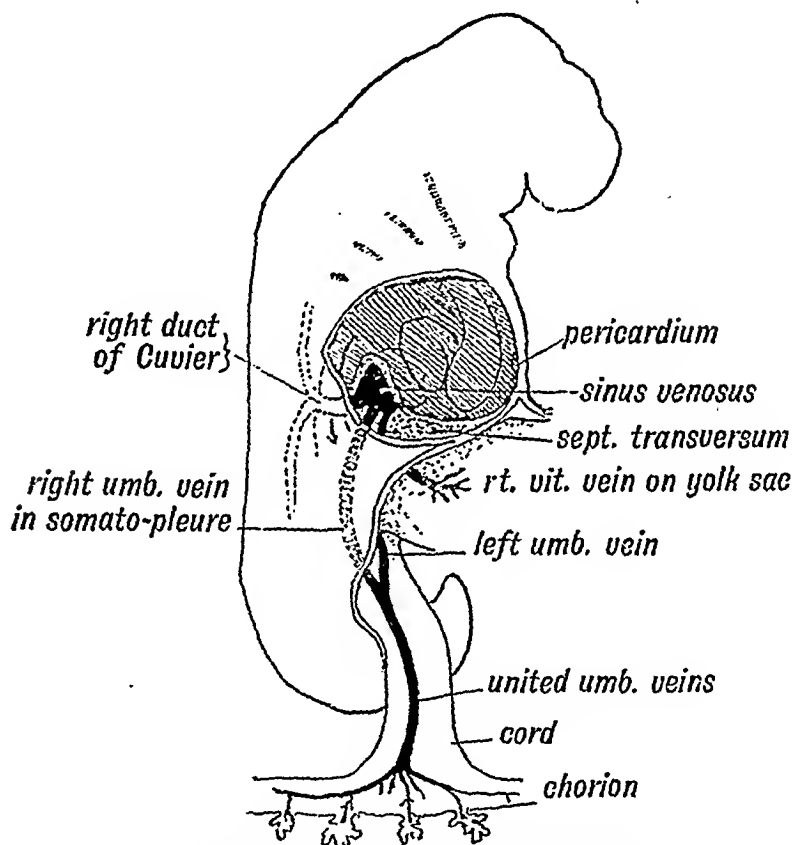


FIG. 383. Diagram of the Right Umbilical Vein of a 5th-week Embryo before the Out-growth of the Liver Trabeculae. (Modified from His.)

individual organs such as the stomach [7]. Angioblastic cells are being transformed into vascular structures at the end of the 3rd and beginning of the 4th week, and although vascularization proceeds at an extremely rapid pace, it is late in the 4th week before the heart begins to beat as a single organ and an effective circulation is being established.

Cardiac Tubes and Pericardium.—In Fig. 384 is shown a coronal section of the head region of a human embryo in which the neural canal is still open and in which only six body segments are demarcated—about the beginning of the 4th week. The cardiac tubes are seen in process of

fusion. Under the fore-gut are seen the angioblastic cells, representing the endothelial lining of the heart; the walls of the tubes clearly represent foldings of the visceral layer of the mesoderm—for they are seen to be still continuous with the mesodermal covering of the fore-gut. The pericardial part of the coelomic space is already formed. It came into existence during the latter part of the 3rd week—by a process of cleavage that separated the mesoderm lying under the fore-gut into visceral and somatic layers. While the heart tubes are separated from the somatic or parietal layer of mesoderm, they remain attached to the floor of the fore-gut by the *dorsal mesocardium*. No ventral mesocardium is formed. Sections showing the evolutionary origin of the pericardium and of the mesodermal wall of the heart are shown in Figs. 180, 384 and 433.

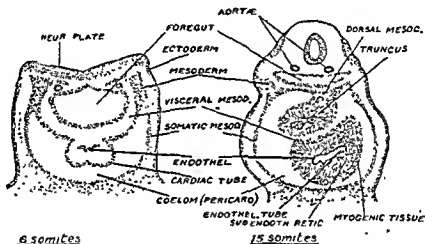


FIG. 384

FIG. 385.

FIG 384. Coronal section of Pericardial Region of a Human Embryo with 6 somites—beginning of 4th week. (After Tandler)

FIG 385. Coronal section of Pericardial Region of a Human Embryo with 15 somites—end of 4th week. (After Tandler)

In Fig. 385 a corresponding section of an embryo a few days older is represented. The process of fusion is complete and already the cardiac tube has become elongated and bent so that it is laid open in the section at two places—near where it enters the floor of the fore-gut, to which it is bound by the dorsal mesocardium, and across the segment that will become the ventricles. The angioblastic mesenchyme now forms the endothelial lining of a narrow cardiac lumen; the outer wall—derived from the visceral mesoderm—represents the muscular and epicardial strata, but as yet, although its cells are contractile, they are still in a myoblastic state. Between endothelial and mesodermal strata is interposed a thick subendothelial reticulum. Into this subendothelial tissue the myoblastic cells will proliferate and establish a myocardial

sponge-work. The spaces of the reticulum are laden with a jelly-like substance.

In Fig. 384 the foundation of the heart is shown in section; in Fig. 386 a reconstruction of the same stage of development is depicted, the cardiac rudiment being viewed on its ventral aspect. In Fig. 386, *A*, the process of fusion of the right and left halves has begun: right and left systems can be demarcated into auricular, ventricular, bulbar and aortic segments; the sinus venosus is not yet differentiated. Fusion takes place in a cranio-caudal direction, the first part to unite being the ventriculo-bulbar, then the auricular and later the venous sinuses. Pulsation is seen first in the bulbo-ventricular segment, the rhythm of the left half being dominant. Pulsation in the auricles soon

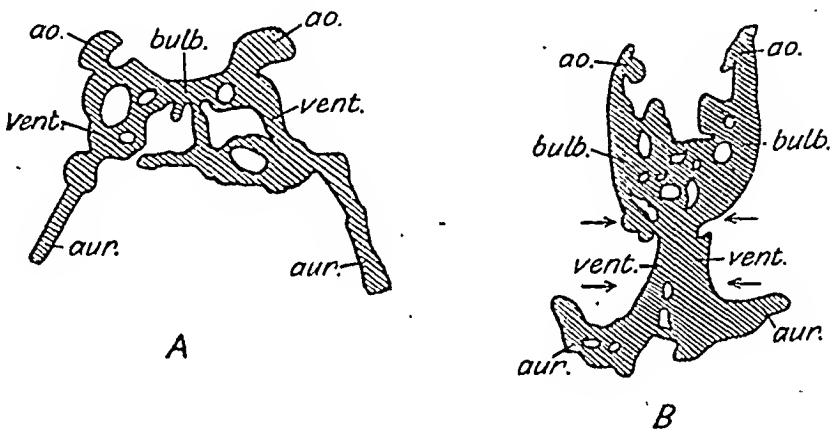


FIG. 386.

- A.* The Cardiac Endothelial Channels of a Human Embryo at the beginning of the 4th week of development. The right and left elements are in the process of fusion. (Orts Llorca.)
- B.* A more advanced stage in which the Ventricular Segments have fused. (N. W. Ingalls.)
- ao.*, ventral aortae; *bulb.*, bulbar segment; *vent.*, ventricular segments; *aur.*, auricular segments. The arrows indicate areas of fusion.

appears; then in the sinus, the latter becoming the pace-maker for the whole heart [8].

Arterial and Venous Mesocardia.—The manner in which the tubular cardiac pump is fixed to the wall of the pericardium in a human embryo in the 4th week of development is shown in Fig. 387. The myocardial wall has been stripped off, showing the endothelial lining of the tube. The heart is fixed at two points only—behind at the place where its first chamber, the sinus venosus, is embedded in the septum transversum, and in front, where its terminal segment, the truncus arteriosus, perforates the roof of the pericardium to enter the wall of the pharynx. At these two points of attachment the epicardial covering of the cardiac tube becomes continuous with the lining membrane of the pericardial cavity; the posterior reflection, on the sinus venosus, is the venous

mesocardium, the anterior, enclosing the truncus, is the *arterial mesocardium*. The rest of the heart is free within its bursa—the pericardial cavity. For a brief interval there is a dorsal mesocardium, but by the middle of the 4th week only a trace remains on the dorsal wall of the pericardium between the two points of attachment (Fig. 387). At no time is there a ventral mesocardium. The iter venosum leading from the pericardial to the pleuro-peritoneal cavity is still open; the cardiac tube has grown in length and assumed certain definite bends and twists.

A week later, as shown in Fig. 388, the arterial mesocardium has shifted backwards along the roof of the pericardium and become approxi-

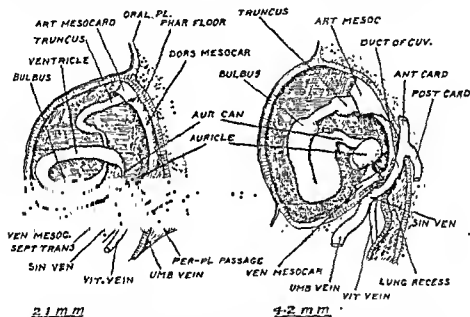


FIG. 387.

FIG. 388

FIG 387. The Attachments of the Cardiac Tube—merely its lining membrane is depicted.—in a Human Embryo 2.1 mm. long and in the 4th week of development (After His)

FIG 388. The Attachments of the Heart in a Human Embryo 4.2 mm. long and in the 5th week of development. As in the preceding figure, only the endothelial lining is represented (After His)

mated to the venous mesocardium. There have also been changes in the hinder attachment, for the septum transversum, which is also migrating backwards, has taken up a more oblique position, being now partly on the dorsal wall. The iter venosum, which is reduced in size, is now crossed by the vein or duct of Cuvier, in a slanting direction. By the 3rd month the mesocardia have approximated and the heart has become fixed in its final position (Fig. 413).

Bends, Twists and Primary Chambers.—In the previous paragraph we have seen how the arterial and venous mesocardia become approximated,

thus bringing together the ends of the original simple cardiac tube. We are now to see that, during the approximation of its ends, certain structural changes take place in the cardiac tube itself, whereby its auricular (atrial) segment is brought in contact with its terminal or aortic segment. The bends, twists and evaginations of the cardiac tube are easily understood if the reader keeps in mind the manner in which the curvatures of the stomach are produced—namely, by unequal growth. The asymmetry of the stomach is due to a more rapid growth along its greater curvature and to the localized expansion which gives rise to the fundus. In some animals there is an actual reduction—an absorption—of the lesser curvature which brings the pylorus in contact

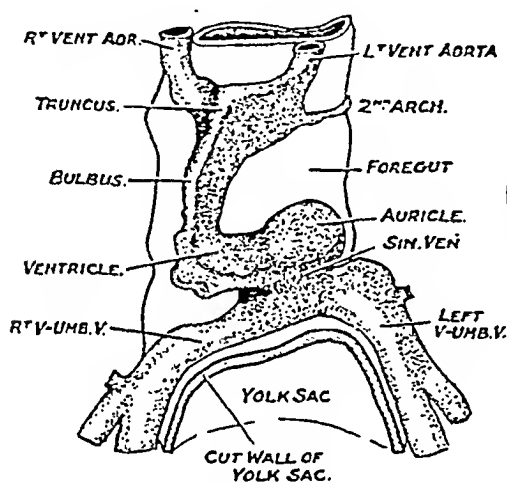


FIG. 389.

FIG. 389. The parts of the Human Heart as seen on their ventral aspect, early in the 4th week. Only the endocardial lining is represented. (After Veit and Esch.)
r-umb. v., vitello-umbilical vein.

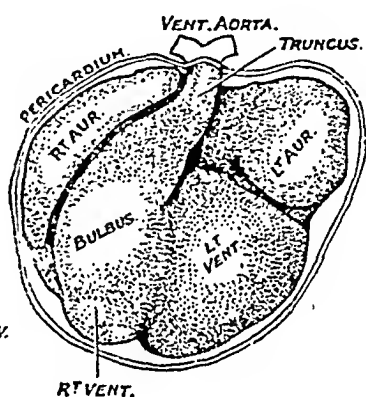


FIG. 390.

FIG. 390. A ventral view of the Heart late in the 5th week of development. (After Prof. Frazer.)

with the oesophagus. The bends, twists and evaginations of the cardiac tube are produced in a similar manner; they are expressions of asymmetrical growth leading up to the stage reached in the fully developed heart.

In Fig. 389 the embryonic heart, early in the 4th week of development, is seen on its ventral aspect and already the primitive ventriculo-bulbar segment of the tube shows a "greater curvature" towards the right and a sharply bent "lesser curvature" towards the left. These curvatures are also shown in Figs. 387 and 388; the ends of the primitive ventricular segment are being approximated. The limb of the ventricular loop nearest the beginning of the heart, the proximal limb, will give rise to the 3rd or *ventricular* chamber of the heart; the distal limb will produce the 4th chamber of the heart—the *bulbus cordis*. Besides the

ventricular, there is another important curvature at the junction of the auricular with the ventricular segment. The lesser curvature—the sharp angle—of this auriculo-ventricular bend is on the right and ventral aspect of the tube (Fig. 389). The 2nd chamber of the heart—the *auricular* or *atrial*—is scarcely marked in the early part of the 4th week (Fig. 389), but by the 5th week evaginations are produced on its dorsal side—at the side opposite to the auriculo-ventricular bend (Figs. 388, 390). The *sinus venosus* or 1st chamber of the heart is partly embedded in the septum transversum in the 4th week, while the *truncus arteriosus* or 5th segment [9] of the cardiac tube, which is elongated in the 4th week,

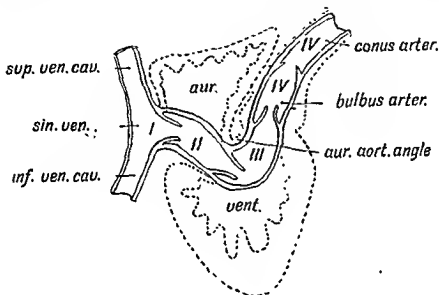


FIG. 389.

is greatly shortened by the 5th (Fig. 390). Further, it will be observed that even in the 4th week (Fig. 387) there are two constricted segments in the endothelial lining of the cardiac tube: one between the auricular and ventricular segments, the auricular canal; and one between the bulbus and truncus, the bulbar canal. All of these five parts of the cardiac tube are to be seen in the heart of a fish (Fig. 391) such as the shark. The sinus venosus serves as a blood reservoir; the auricle acts as a pump to feed the ventricles, the ventricle is the pump of the gills and body; the bulbus, which becomes incorporated in the right ventricle of the mammalian heart, feeds the gills in diastole, the truncus serves purely as a canal.

The *Sinus Venosus*, the first chamber of the vertebrate foetal heart, is

formed by the union of the vitelline veins ; the umbilical veins and ducts of Cuvier come subsequently to open in it (Fig. 392). The ducts of Cuvier reach it from the somatopleure by passing round the coelomic passages (Figs. 387, 388) and entering the septum transversum. In fish and in the human embryo the sinus serves as a reservoir during systole of the auricle ; the systolic wave always commences in the sinus venosus when all parts of the heart are completed. The right and left *venous valves* (Fig. 394) at the junction of the sinus and auricle prevent the regurgitation of blood during systole of the auricle. These valves

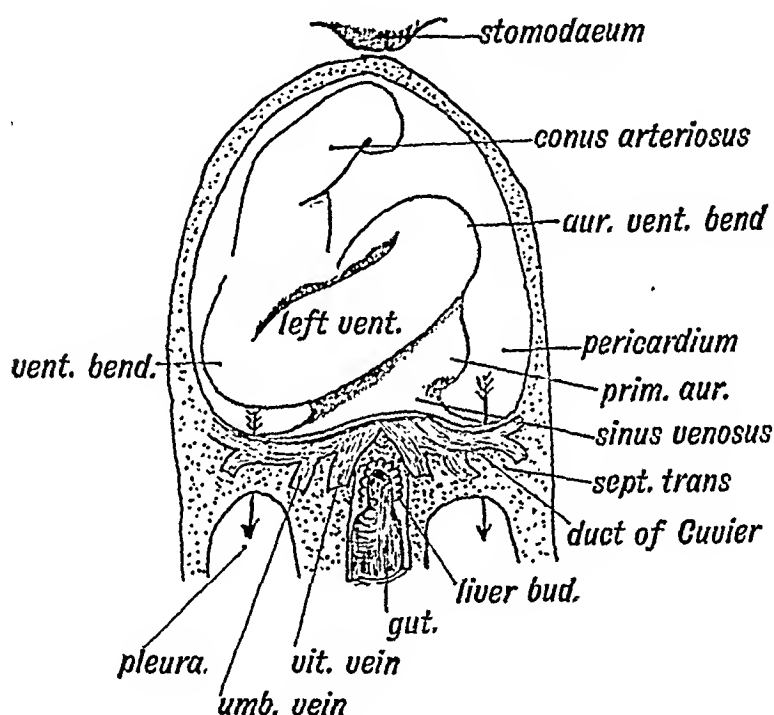


FIG. 392. Showing the two chief Bends that occur in the Heart during the 4th week. Conus arteriosus, now usually known as the truncus arteriosus. The arrows are in the pleuro-pericardial passages.

become more or less atrophied when the right and left sides of the heart are completely separated by the formation of septa.

Fate of the Sinus Venosus (Fig. 393).—Since the sinus venosus plays such a dominant part in the physiology of the heart of lower vertebrates, it is extremely important that we should follow its fate in the human heart. It becomes submerged chiefly in the right auricle, the sulcus terminalis (see Fig. 396) marking the line at which it becomes included by the upgrowth of auricular tissue. Already, at the end of the 5th week, the orifice of the sinus has come to occupy a position in the posterior or dorsal wall of the right part of the common auricle (Fig. 394). The part of the right auricle that it forms is indicated by the entrance

of the following vessels, all of them being originally tributaries of the sinus: (i) the superior vena cava (the right duct of Cuvier); (ii) the

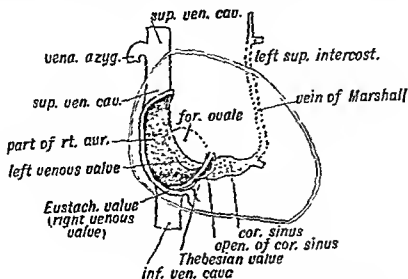


FIG. 333. Showing the part of the Right Auricle formed from the Sinus Venosus.

inferior vena cava, which also opens into the sinus; (iii) the oblique vein of Marshall (left duct of Cuvier), which opens into the left horn of

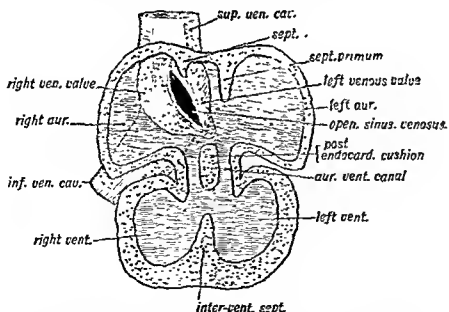


FIG. 334. Section of the Heart of a 6th-week Human Embryo showing the Right and Left Venous Valves that guard the Entrance of the Sinus Venosus into the Primitive Auricle (After His)

the sinus venosus. The left horn of the sinus becomes the coronary sinus. The sulcus terminalis is marked on the interior of the right auricle by a strong muscular band (taenia terminalis), which runs down

formed by the union of the vitelline veins ; the umbilical veins and ducts of Cuvier come subsequently to open in it (Fig. 392). The ducts of Cuvier reach it from the somatopleure by passing round the coelomic passages (Figs. 387, 388) and entering the septum transversum. In fish and in the human embryo the sinus serves as a reservoir during systole of the auricle ; the systolic wave always commences in the sinus venosus when all parts of the heart are completed. The right and left *venous valves* (Fig. 394) at the junction of the sinus and auricle prevent the regurgitation of blood during systole of the auricle. These valves

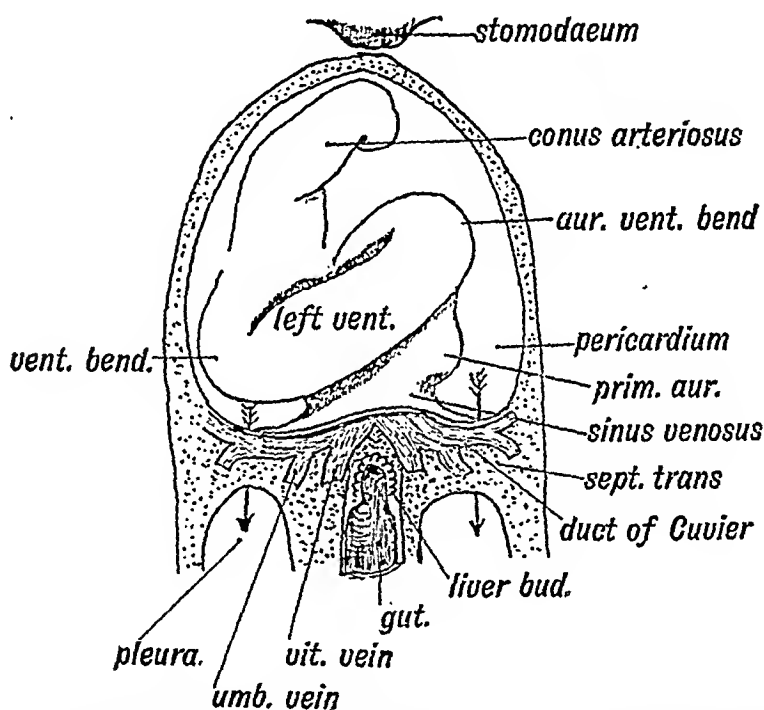


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caval orifice, (ii) a band of musculature accompanying this remnant (Fig. 395).

The **Limbic Bands** are two inflections of the wall of the sinus venosus that are formed (a) between the superior and inferior caval orifices, (b) between the inferior caval orifice and that of the coronary sinus [10]. In these inflections bands of auricular musculature cross, forming the upper and lower limbic bands (Fig. 395). Thus the mechanical valves that prevent auricular regurgitation in low vertebrates are replaced by a muscular mechanism which serves the same purpose. In amphibians and reptiles, where the division of the heart is incomplete, over-pressure in the right side is relieved by the escape of blood to the left side of the heart; but in birds and mammals such an adjustment is impossible, hence the mechanical venous valves are replaced by a "safety mechan-

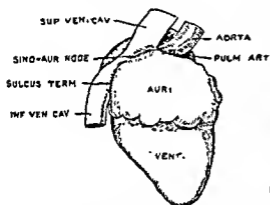


FIG. 396.

FIG. 396. Human Heart at the beginning of the 3rd month of development, to show the position of the Sino-auricular Node. The unsubmerged strip of sinus venosus is seen between the superior and inferior venae cavae.

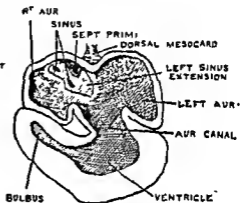


FIG. 397.

FIG. 397. The Posterior Wall of the Common Auricle of an Embryo of the 5th week, showing the Left Extension of the Sinus Venosus. (His)

ism," which will allow regurgitation from the auricles to the veins if the right side becomes over-distended.

Sino-auricular Node [11].—The musculature of the sinus venosus of fishes is made up of small peculiar fibres rich in nuclei and in nerve supply. It has, more than all the musculature of the heart, the power of automatic rhythmical contraction. In human and mammalian hearts the sinus musculature is replaced by fibres similar to those of the auricle—all but at the sulcus terminalis, which marks the junction of the sinus and auricle. In the sulcus, just in front of the termination of the superior vena cava (Fig. 396), an area of primitive fibres persists—the sino-auricular node. It becomes differentiated in the human embryo towards the end of the 6th week; the auriculo-ventricular node appears about a week earlier. In lower mammals like the mole, the sino-auricular tissue

on the anterior wall of the right auricle from the superior to the inferior vena cava, and indicates the junction of the primitive auricle with the sinus venosus (Fig. 395). The musculature which surrounds the terminal part of the superior vena cava and that contained in the wall of the coronary sinus represents the musculature of the sinus. Elsewhere the muscle of the sinus appears to be replaced by that of the auricle.

Valves of the Sinus Venosus.—Right and left valves (venous valves) guard the entrance of the sinus to the primitive auricle and prevent the regurgitation of blood when the auricle contracts (Fig. 394). The valves meet above and form a *superior fornix* in front of the superior caval

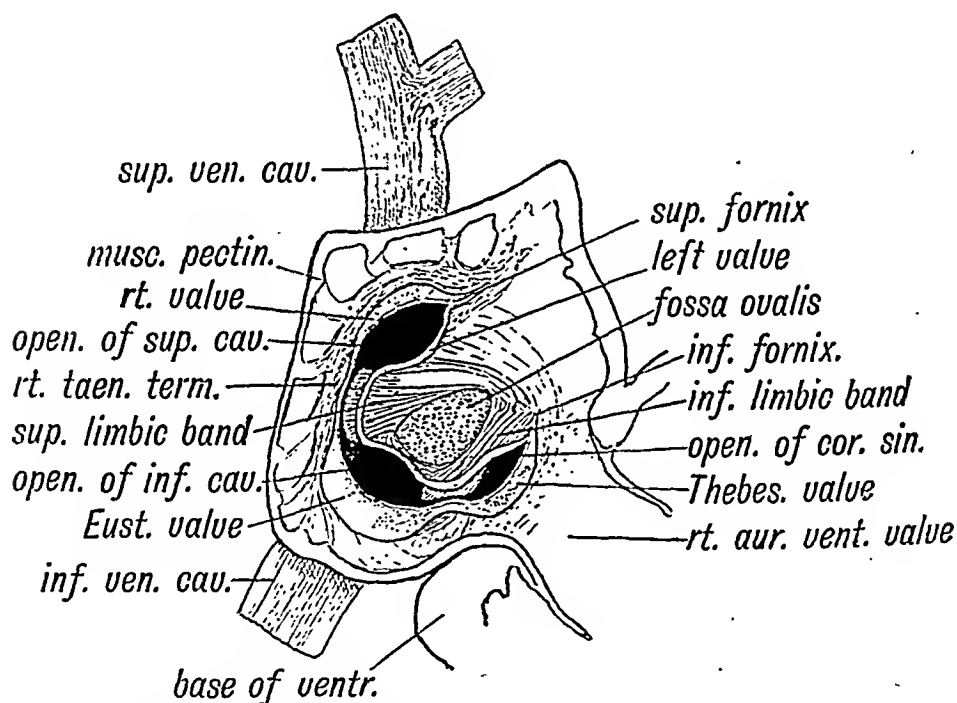


FIG. 395. Diagram of the Right Auricle thrown open to show the position and relations of the Right and Left Venous Valves and the manner in which they are broken up by the Superior and Inferior Limbic Bands.

opening (Fig. 394, *sept.*); they meet below in an *inferior fornix*, which, owing to the great shortening of the ventral part of the auricular segment, reaches the base of the ventricle, and actually fuses with the posterior endocardial cushion (Fig. 401). This has an important bearing on the origin of the auriculo-ventricular (A.V.) bundle within the auricular canal. Along the base of each valve is arranged a band or taenia of the auricular musculature. Thus each valve consists of a membranous marginal part and a muscular basal part. The right valve in the adult heart becomes (Fig. 395) (i) the Thebesian and (ii) Eustachian valves; (iii) the musculature at its base forms the taenia terminalis. The left valve becomes (i) a fretted membrane on the septal margin of the inferior

arise in a manner similar to the corresponding parts on the right side. In the human heart the vestibule forms a large part of the left auricle, the primitive auricle being reduced to form merely the appendix (Fig. 399). The vestibule is marked off from the rest of the auricle by a prominent muscular fasciculus—the *taenia terminalis sinistra*.

Origin of the Vestibule of the Left Auricle.—The representative of the pulmonary veins in fishes—viz. the vein of the swim bladder—ends directly or indirectly in the sinus venosus, a condition which may reappear as an abnormality in the human subject. In the Dipnoi, in which the swim bladder serves as a real lung, the pulmonary vein passes along the left wall of the sinus venosus to open in the left auricle near the base of

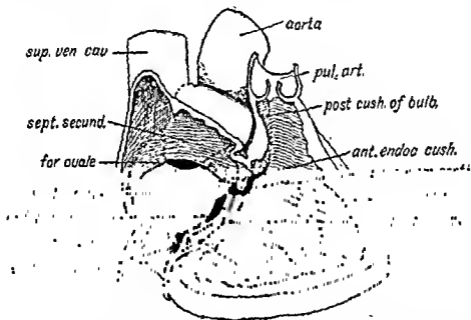


FIG. 400 Diagram of the opened Right Auricle and Ventricle to show the parts which enter into the Formation of the Septum.

the left venous valve in a manner almost identical to that shown in some abnormal human hearts (see Fig. 407). In the human embryo the pulmonary veins meet in the venous mesocardium, and open by a single orifice as in the Dipnoi. As the lungs develop they grow round and overlap the heart; the right and left pulmonary veins separate; their orifices move apart; later the right and left veins subdivide. With these changes the venous mesocardium is widened and the part of the auricle in which the veins end is greatly extended to form the vestibule (compare Figs. 398, 399). It is highly probable that the vestibule of the left auricle also represents an extension of the sinus venosus. The late Prof. His, who laid our knowledge of the development of the human embryo on a sure foundation of fact—he died in 1904—believed this

is more extensive; it extends along the greater part of the sulcus terminalis, and passes towards the pulmonary veins. In amphibia and reptiles it extends to the part of the left auricle (vestibule) in which the pulmonary veins terminate. In the lowest mammals—monotremes—the muscular tissue of the node assumes a peculiar form [12]. Thus the higher in the animal scale one ascends, the greater is the reduction of the sino-auricular nodal tissue. It is in reality a neuro-muscular tissue, and is well defined by the 3rd month of development. Sir T. Lewis found that the contraction of the heart spread from the sino-auricular node, and gave it the name of the “pace-maker” of the heart.

Formation of the Right Auricle.—The right auricle or atrium is formed

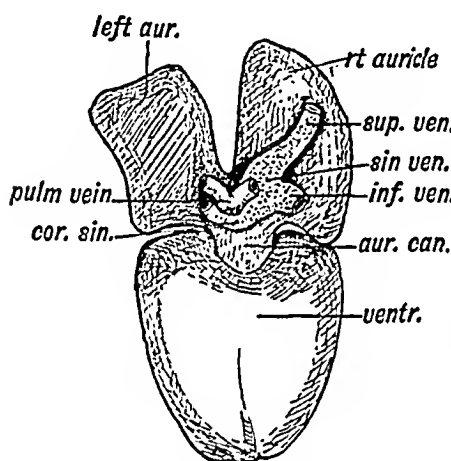


FIG. 398.

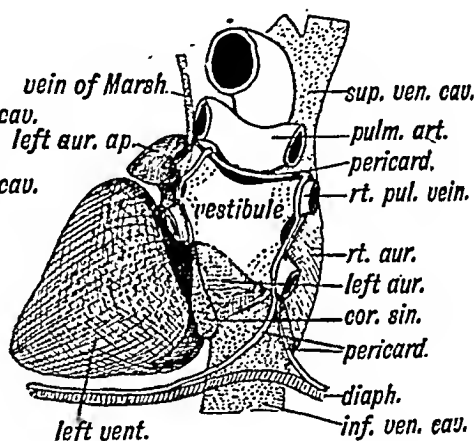


FIG. 399.

FIG. 398. Reptilian Heart, viewed on its dorsal aspect, to show (1) the manner in which the Auricles arise from the Cardiac Tube; (2) the Auricular Canal, (3) the Sinus Venosus and Great Veins, (4) the Common Pulmonary Vein, which, at its termination, is embraced by the sinus venosus.

FIG. 399. Heart of Adult viewed from behind to show the Vestibule and the other parts of the Left Auricle. The auricle was in a state of systole. The remains of the left superior vena cava (vein of Marshall) and the attachment of the pericardium are also indicated.

by the combination of three parts : (i) the right primitive auricle, which appears as a diverticulum from the right dorso-lateral aspect of the auricular segment of the cardiac tube (Fig. 391) (it forms the appendix and all that part of the right auricle which is furnished with *musculi pectinati*) ; (ii) the auricular canal (Fig. 397), which forms the smooth part of the chamber above the bases of the right auriculo-ventricular cusps [13] ; (iii) the sinus venosus, which forms the part of the right auricle between the remnants of the right and left venous valves (Fig. 395).

Formation of the Left Auricle.—The left auricle is also formed by the combination of three parts : (i) the vestibule, which arises as an extension round the terminal parts of the pulmonary veins (Figs. 398, 399), (ii) the left primitive auricle, and (iii) the auricular canal, all of which

cushions; the adjacent margins of the septum and endocardial cushions fuse, but occasionally the fusion is incomplete, an interauricular foramen (*foramen primum*) being left between the bases of the auriculo-ventricular valves below and septum ovale above (Figs. 400, 407). In mammals and birds the upper part of the septum primum breaks down, the *foramen ovale* being thus formed. The part that persists forms the septum ovale. The *septum secundum* (Fig. 400) is formed by an inflection of musculature from the roof of the auricle to the right of the septum primum. It forms the annulus ovalis (limbic bands) and the musculature of the septum above the foramen ovale (Fig. 395). The foramen ovale thus becomes bounded above by the septum secundum, below by the septum primum. In 25% of people, according to Fawcett's statistics, the foramen ovale fails to close within the first year after birth, but even when an opening remains blood could pass from the right to the left auricle only when the pressure was greater in the right than in the left [14]. The foramen ovale is an adaptation to the foetal type of respiration; by it the purer blood returning from the placenta can pass from the right to the left side of the heart without passing through the lungs, which are then only partially pervious.

Divisions of the Truncus Arteriosus.—While the auricular segment of the cardiac tube is undergoing division during the 6th week a similar process is taking place in its terminal segment—the truncus or conus arteriosus, leading to the separation of the pulmonary from the systemic aorta. We have seen that the truncus becomes shortened during the 5th week (Figs. 387, 388) and at the same time the ventral aorta or “aortic sac” is being cleft into right and left vessels. In the 6th week the process of cleavage has reached the origin of the 6th pair of aortic arches from which the pulmonary arteries arise (Fig. 431), so that there now remains but a short segment of the common aortic stem to undergo division and give rise to the intrapericardial parts of the aorta and common pulmonary artery. The first step in the division is the appearance of four endocardial cushions at the commencement of the common aortic trunk (Fig. 402, A), the two larger cushions being placed right and left. As is shown in Fig. 402, these cushions become, for the chief part, converted into the aortic and pulmonary valves—but two of them, the right and left, become fused and assist in forming the spiral septum which separates the aortic from the pulmonary passage. By the end of the 6th week the process of cleavage has spread towards the heart; the lateral cushions are divided as shown in Fig. 402, B; henceforth the pulmonary artery and aorta form distinct channels. We have here another example of what may be called developmental surgery.

Bulbus Cordis.—We have seen how the first chamber of the heart—the

to be the case. It is certainly so in the heart of amphibians. In Fig. 397 the sinus area will be seen to extend into the posterior wall of the left auricle. It is on this left extension that the venous channels from the lung buds open.

Auricular Septa.—During the 6th week the auricular part of the heart becomes separated into right and left chambers by the formation and union of the three following elements: (i) the endocardial cushions, (ii) the septum primum, (iii) septum secundum. Two *endocardial cushions* arise as thickenings of the endocardium of the common auricular canal, one on its dorsal or posterior wall, the other on its ventral or anterior wall; they meet and fuse, and thus divide the common auricular

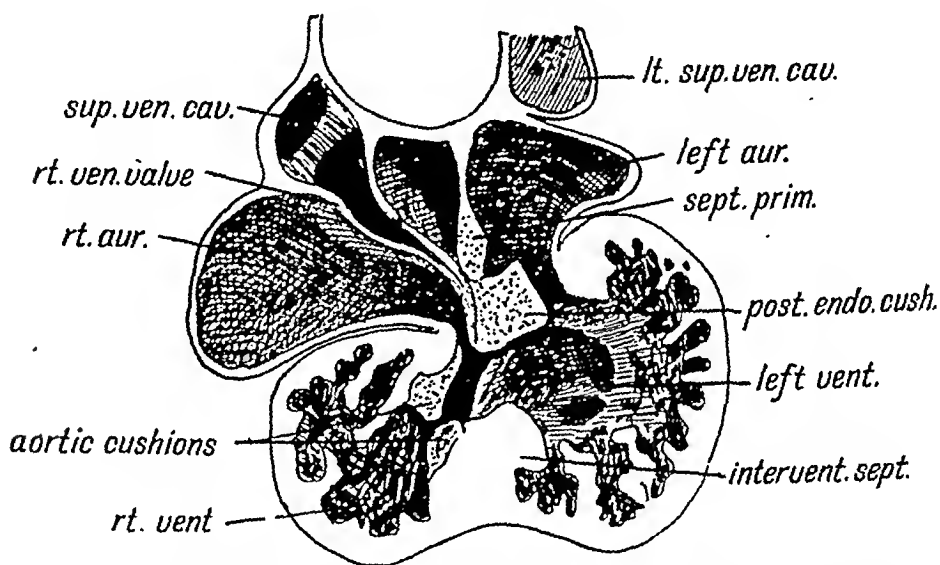


FIG. 401. Coronal section of the Heart of a Rabbit, illustrating the condition of parts in the 6th week of human development. (Born.)

"Aortic cushions" = bulbar cushions.

canal into the right and left auriculo-ventricular orifices (Fig. 401). In amphibians the endocardial cushions form the dorsal and ventral cusps of the common auriculo-ventricular valve; in reptiles these two cusps become united, and thus divide the common auriculo-ventricular orifice into the right and left channels; in birds and mammals their fusion is complete. The lower fornix of the venous valves (Figs. 394, 401) becomes implanted on the posterior cushion; thus the sinus comes almost to reach the brim of the ventricular chamber. The *septum primum* (Fig. 400) appears at the beginning of the 6th week as a crescentic fold on the roof of the primitive auricle, and while it may actually grow downwards, yet appears to be produced mainly by the expansion of the two auricular chambers (Fig. 401). Its lower margin, which is covered by a thickening of endocardial tissue, is attached to both endocardial

cushions; the adjacent margins of the septum and endocardial cushions fuse, but occasionally the fusion is incomplete, an interauricular foramen (*foramen primum*) being left between the bases of the auriculo-ventricular valves below and septum ovale above (Figs. 400, 407). In mammals and birds the upper part of the septum primum breaks down, the *foramen ovale* being thus formed. The part that persists forms the septum ovale. The *septum secundum* (Fig. 400) is formed by an inflection of musculature from the roof of the auricle to the right of the septum primum. It forms the annulus ovalis (limbic bands) and the musculature of the septum above the foramen ovale (Fig. 395). The foramen ovale thus becomes bounded above by the septum secundum, below by the septum primum. In 25% of people, according to Fawcett's statistics, the foramen ovale fails to close within the first year after birth, but even when an opening remains blood could pass from the right to the left auricle only when the pressure was greater in the right than in the left [14]. The foramen ovale is an adaptation to the foetal type of respiration; by it the purer blood returning from the placenta can pass from the right to the left side of the heart without passing through the lungs, which are then only partially pervious.

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Bulbus Cordis.—We have seen how the first chamber of the heart—the

sinus venosus—becomes included in the auricles. In a somewhat similar manner the 4th chamber of the heart—the bulbus cordis—becomes submerged in the ventricles, principally in the right ventricle [15]. In

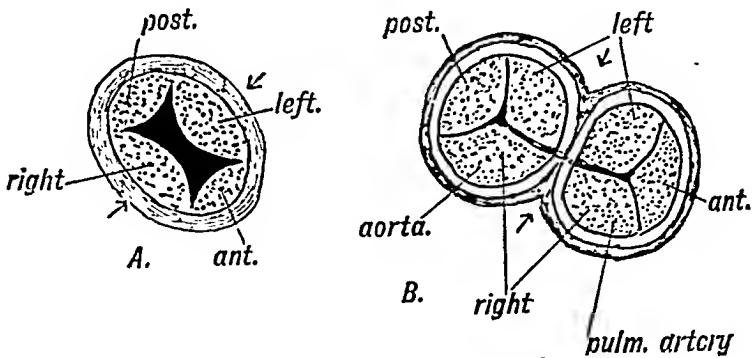


FIG. 402. The Origin of the Semilunar Valves.

A. The four Endocardial Cushions of the Truncus Arteriosus.

B. The division of the Lateral Cushions to form two Aortic and two Pulmonary Semilunar Valves.

Figs. 403 and 404 the heart of a human embryo and that of a shark are placed side by side. In both, the truncus arteriosus and ventral aorta are present, 1; the bulbus cordis, 2; it is lined with valves in the shark

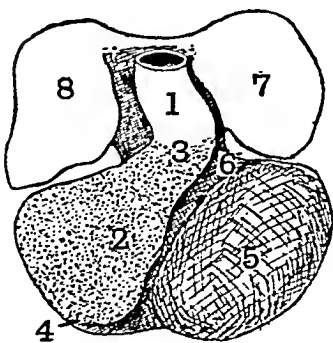


FIG. 403.

FIG. 403. Heart of an Embryo of 4 weeks seen from the front. (After His.) Explanation in text.

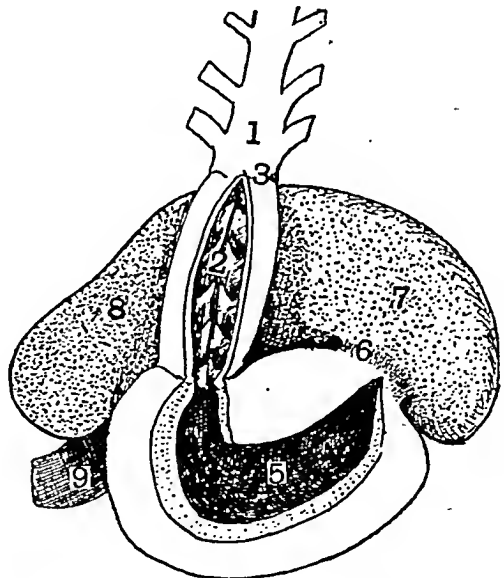


FIG. 404.

FIG. 404. Heart of a Shark viewed from the front.

and surrounded by cardiac musculature; the bulbus is distinctly marked off from the ventricle at 4, and from the truncus at 3. The ventricle, 5, in the shark has the shape of a stomach; in the embryonic human heart a diverticulum or evagination indicating the left ventricle has already

appeared (4th week); the auricular canal, 6, the left and right auricles 7, 8, are also present. Thus in the human embryo all the parts of the primitive vertebrate heart are represented.

Fate of the Bulbus Cordis.—The fate of the bulbus cordis is most easily understood by a reference to diagrams such as are represented in Figs. 405, A, B. The bulbo-ventricular part of the heart in the human embryo resembles the stomach: there is a greater and a lesser curvature. In the 2nd month the lesser curvature, represented in the diagram by a heavy black line, undergoes a process of atrophy. The result is (Fig. 405, B) that the cavity of the bulbus becomes thrown into that of the ventricle and the auriculo-ventricular and aortic orifices are brought side by side. At this time, when the lesser curvature is disappearing, the

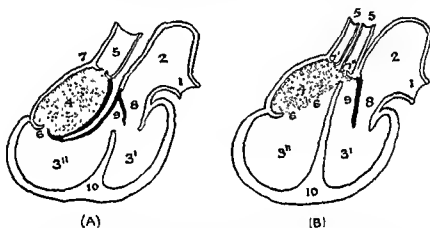


FIG. 405

A. Diagrammatic section of the Embryonic Heart in the 4th week.

B. Diagrammatic section of the Foetal Heart at the 3rd month

1, sinus venosus; 2, auricle; 3', 3'', left and right ventricles; 4, bulbus cordis; 5, common aorta; 6, bulbo-ventricular junction; 7, bulbo-aortic junction; 8, auriculo-ventricular junction; 9, ant. cusp. of mitral; 10, base of intervent. sept.

cavities of the ventricles are undergoing an enlargement by an evagination of the ventricular wall, leaving the interventricular septum between the evaginations (Figs. 394, 401). The conus or truncus arteriosus is dividing then into systemic and pulmonary aortae. Thus it comes about that the cavity of the bulbus cordis is converted into the infundibulum of the right ventricle, merely a trace extending across to the left ventricle above the interventricular septum. The importance of recognizing the bulbus cordis as a separate constituent of the heart will be realized when it is remembered that 95% of the cases of congenital malformation are the result of its imperfect transformation to form the infundibulum of the right ventricle of the heart. In nearly every case of *congenital stenosis* of the pulmonary orifice, a cavity of variable size will be found under the malformed valves representing the bulbus cordis. In fishes the bulbus

is concerned with the blood supply to the gills ; its derivative, the infundibulum of the right ventricle, has to do with the regulation of the blood supply to the lungs, but in neither case do we know the exact function of this part of the heart.

Bulbar Cushions.—During the transformation of the bulbus in the 6th week, there appear within it two endocardial cushions—evolved from the series of valves that line the bulbus of the primitive heart (Fig. 404). The part taken by them in building up the interventricular septum can best be realized when the infundibular part of the right ventricle is exposed as in Fig. 400. The line of fusion between the posterior and anterior bulbar cushions is seen to descend in the septal wall of the infundibulum from the pulmonary valves to the site of the interventricular foramen [16]. When the bulbar cushions fuse at the

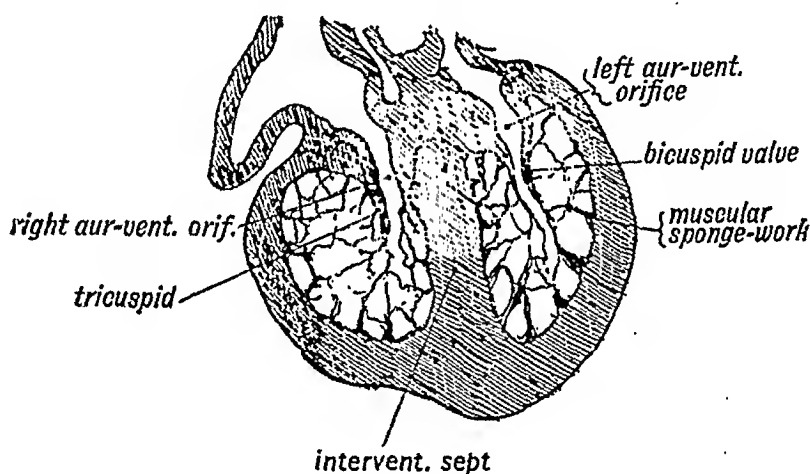


FIG. 406. Section of the Ventricles of the Foetal Heart, showing the Muscular Sponge-work within their Cavities. (After His.)

end of the 6th week the small sub-aortic part of the bulbus included in the left ventricle becomes separated from the main part included in the infundibulum of the right ventricle (Figs. 405, *A*, *B*). The bulbar cushions are shown at an early stage of development in Fig. 401, where they are labelled as "aortic cushions."

Formation of the Ventricles.—Along the lateral and convex aspects of the ventricular tube the musculature grows rapidly, forming a dense superficial layer and a deep sponge-work system of trabeculae, which almost fill the ventricular chamber. In the hearts of fishes and amphibians the sponge-work persists, but in birds and mammals the ventricular chambers are enlarged by the absorption of the sponge-work and the condensation of a parietal stratum. Between the right and left excavations, however, part of the sponge-work is left to form the interventricular septum (Fig. 406). In front the musculature of the septum is attached

to the anterior cushion of the bulbus cordis (Figs. 400, 401); behind, it is attached to the posterior of the two endocardial cushions in the auricular canal. On its upper free crescentic margin is a thickening of endocardial tissue. The closure of the *interventricular foramen* completes the separation of the left from the right ventricle of the heart. The foramen is bounded below by the margin of the interventricular septum; above, by the bulbar cushions; and behind by the a.v. endocardial cushions (Figs. 400, 409). The *pars membranacea septi*, which is found beneath the base of the septal cusp of the tricuspid and below the septal cusps of the aortic valve, is formed towards the end of the 7th week by the fusion of the endocardial margins of the interventricular foramen [17]. The foramen is thus closed by that process to which the name of *zygosis* has been given (p. 407). Only in mammals and birds is the interventricular foramen closed, a foramen ovale established in the auricular septum, and the venous valves replaced by a muscular mechanism.

Coronary Circulation [18].—A section of the ventricular wall in the 4th week of development (Fig. 385) shows three strata: (a) an endothelial lining or endocardium, (b) a thin outer or epicardial stratum in which muscle cells are formed, (c) a thick intermediate zone, made up of delicate fibres embedded in a jelly-like substance. During the 5th, 6th and 7th weeks muscle fibres, produced in the epicardial stratum, invade the intermediate zone and form a sponge-work almost filling the ventricular cavities. The sponge-work draws its nourishment directly from the blood by which it is bathed. In the 7th week the epicardial zone produces its new fibres so that they form a dense layer, no longer accessible to intra-ventricular blood. With the condensation of the ventricular musculature arose the need for a special blood supply, that furnished by the coronary arteries. In the 6th week the right and left coronary arteries arise as vascular buds, emerging from the root of the aorta. The coronary veins arise as outgrowths from the coronary sinus. By the end of the 2nd month an effective coronary circulation has been established.

During foetal life new muscle fibres are being produced, older fibres are being replaced. This process of renewal goes on not only in childhood but also in adult years [19]. Everywhere the muscle cells of the heart branch and establish union with neighbouring cells. From their first appearance the muscle cells of the heart are rhythmically contractile. The heart is a contractile organ before nerve cells or nerve fibres reach it.

Abnormalities of the Heart.—Five elements enter into the formation of the septum of the heart: the two interauricular septa, the two endocardial cushions of the auricular canal, the interventricular septum, the endocardial cushions of the bulbus and the cushions of the bulbus cordis

is concerned with the blood supply to the gills ; its derivative, the infundibulum of the right ventricle, has to do with the regulation of the blood supply to the lungs, but in neither case do we know the exact function of this part of the heart.

Bulbar Cushions.—During the transformation of the bulbus in the 6th week, there appear within it two endocardial cushions—evolved from the series of valves that line the bulbus of the primitive heart (Fig. 404). The part taken by them in building up the interventricular septum can best be realized when the infundibular part of the right ventricle is exposed as in Fig. 400. The line of fusion between the posterior and anterior bulbar cushions is seen to descend in the septal wall of the infundibulum from the pulmonary valves to the site of the interventricular foramen [16]. When the bulbar cushions fuse at the

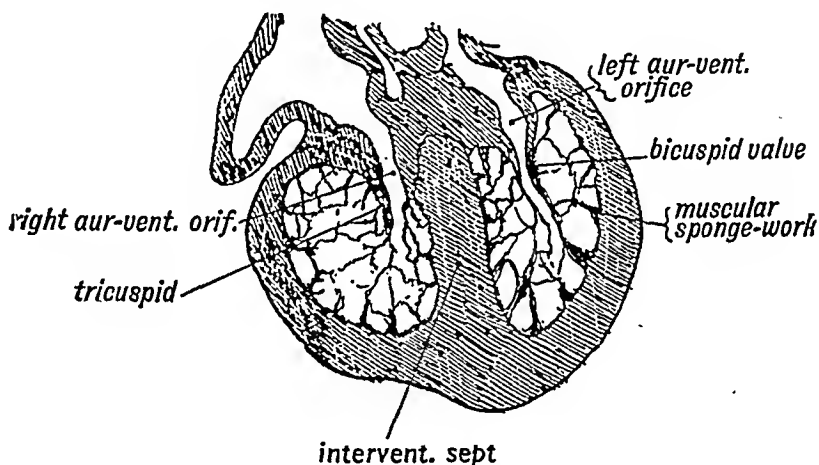


FIG. 406. Section of the Ventricles of the Foetal Heart, showing the Muscular Sponge-work within their Cavities. (After His.)

end of the 6th week the small sub-aortic part of the bulbus included in the left ventricle becomes separated from the main part included in the infundibulum of the right ventricle (Figs. 405, *A*, *B*). The bulbar cushions are shown at an early stage of development in Fig. 401, where they are labelled as “aortic cushions.”

Formation of the Ventricles.—Along the lateral and convex aspects of the ventricular tube the musculature grows rapidly, forming a dense superficial layer and a deep sponge-work system of trabeculae, which almost fill the ventricular chamber. In the hearts of fishes and amphibians the sponge-work persists, but in birds and mammals the ventricular chambers are enlarged by the absorption of the sponge-work and the condensation of a parietal stratum. Between the right and left excavations, however, part of the sponge-work is left to form the interventricular septum (Fig. 406). In front the musculature of the septum is attached

Various maldevelopments of the heart throw light on the nature of the auriculo-ventricular valves. In Fig. 407 an abnormality of this kind is represented. The anterior and posterior endocardial cushions have not united, hence the tricuspid and mitral valves are continuous across the upper border of the septum (Fig. 408). The aperture seen above the interventricular septum is the *foramen primum*—not the interventricular foramen.

Nerves of the Heart.—The development of nerves of the heart has been investigated recently by several anatomists [22]. The heart begins to beat late in the 3rd week; nerve fibres, from vagus and sympathetic, do not begin to invade the heart until the end of the 4th week. The invasion of cells and fibres takes place through (i) the venous mesocardium to the atrial end of the heart, giving special supplies to sino-auricular and atrio-ventricular nodes; (ii) through the arterial mesocardium to the bulbar end of the heart. No nerve cells occur on the ventricular side of the atrio-ventricular groove (Woollard) [23].

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- [5] For anomalies of veins, see references to Franklin and to Poynter in note [3] and to Maxwell and Erwin in note [4].
- [6] Scammon and Norris, *Anat. Rec.*, 1918, 15, 165.
- [7] It is estimated that the heart forms one-tenth of the total weight of the embryo in the 5th week.
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(Fig. 400). Abnormalities may result from their non-union, but by far the commonest defect found is a patency of the interventricular foramen (Fig. 409). This is accompanied in nearly every case by an arrest in the expansion of the bulbus cordis and a stenosis or narrowing at the orifice of the pulmonary artery (*congenital pulmonary stenosis*). The blood of the right ventricle, in such cases, is pumped into the aorta, through the interventricular foramen; blood is supplied to the lungs through the ductus arteriosus or by the bronchial arteries from the aorta [20]. Amongst the most difficult to explain are the abnormalities of trans-

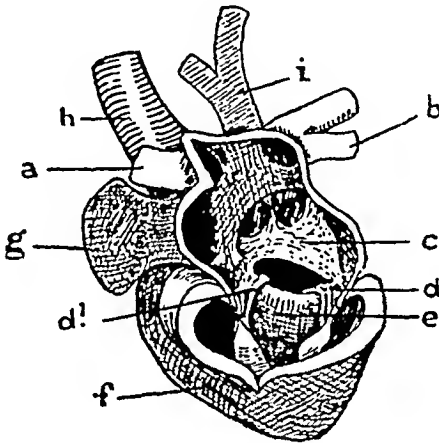


FIG. 407.

Fig. 407. Abnormal Heart of a Child with the Left Auricle and Ventricle laid open. *a*, left, *b*, right pulmonary veins; *c*, septum primum; *d*, *d'*, posterior and anterior endocardial cushions; *e*, interventricular septum; *f*, left ventricle; *g*, left auricular appendix; *h*, aorta; *i*, sup. vena cava.

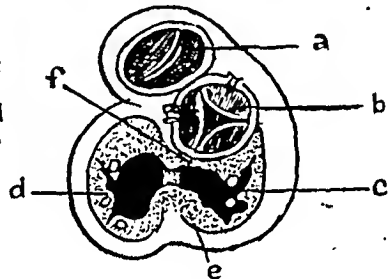


FIG. 408.

Fig. 408. Same Heart from above. *a*, the orifice of pulmonary artery with fusion of septal cusps; *b*, valves of aorta, with the coronary arteries rising above septal cusps; *c*, *d*, *e*, *f*, continuity of the tricuspid and mitral valves across the upper border of septum.

position—where the aorta takes the anterior position of the pulmonary artery, and that artery, the posterior position of the aorta [21].

Auriculo-Ventricular Valves.—At first the auricular canal is exposed on the surface of the heart (Fig. 403), but it soon becomes enveloped by the upgrowth and excavation of the bases of the ventricles (Fig. 397). The auricular canal, with an attenuated envelopment derived from the ventricle, thus comes to hang within the ventricular chambers and forms the lateral cusps of the tricuspid and mitral valves (Fig. 406). The septal cusps are formed from processes of the endocardial cushions (Fig. 406). The anterior cusps of the tricuspid has added to it a large element from the anterior bulbar cushion (Odgers). The chordae tendineae, musculi papillares, columnae carnae, trabeculae and moderator band are derived from the muscular sponge-work of the ventricles.

CHAPTER XXIII

CIRCULATORY SYSTEM (continued)

Purkinje System of the Heart.—About the middle of the 19th century, Purkinje, Professor of Anatomy at Breslau, discovered large peculiar muscle fibres beneath the endocardium of the heart of the sheep and of other ungulate animals. In 1906 Tawara showed that such fibres were connected with a muscular hundle which rose in the wall of the auricle the orifice of the coronary sinus and entered the ventricle along the upper border of the interventricular system [1]. In many cases of malformed heart the primitive relations of the *auriculo-ventricular* (a.v.) *bundle* may be seen (Fig. 409). It passes along the upper border

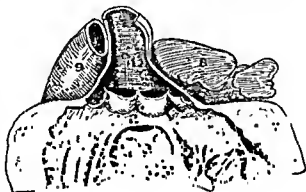


FIG 409. The Auriculo-ventricular Bundle in a Heart with open Interventricular Foramen. 1, 2, division issuing septum (4); 5, ventricle; 6, left auricle; 7, pulmonary artery.

of the interventricular septum below the interventricular foramen. Its left branch descends on the septum to the musculi papillares of the left ventricle; the right division or branch passes along the moderator band, which marks the junction of the bulbus cordis with the body of the right ventricle. When it is remembered that the ventricles arise from evaginations of the ventricular tube, it will be seen that the bundle on the upper border of the septum occupies the least disturbed part of the lumen of the primitive cardiac tube [2].

The evolution of the Purkinje system may be realized from a study of Fig. 410. Gaskell found in 1883 that the auricles and ventricles were connected in fishes, amphibians and reptiles by the musculature of the

N., *Zeitsch. Anat. Entwickl.*, 1934, 103, 813; Gátzi, W., *Archiv. d'Anat. Hist.*, 1929, 10, 371; Walmsley, Robert, *Contrib. Emb.*, 1938, No. 164 (venous valves in foetal finback whale).

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[20] See references given in note [17].

[21] For accounts of transposition of stems, see Walmsley, T., *Jour. Anat.*, 1931, 65, 528; Spitzer, A., *Virchow's Archiv.*, 1933, 289, 247; Pernkopf and Wirtinger, *Zeitsch. Anat. Entwickl.*, 1933, 100, 563 (analysis of factors concerned); Ingalls, N. W., *Anat. Rec.*, 1932, 52, 269 (dextrocardia).

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[23] Woollard, H. H., *Jour. Anat.*, 1926, 60, 345; Jones, Tudor, *ibid.*, 1927, 61, 247.

CHAPTER XXIII

CIRCULATORY SYSTEM (continued)

Purkinje System of the Heart.—About the middle of the 19th century, Purkinje, Professor of Anatomy at Breslau, discovered large peculiar muscle fibres beneath the endocardium of the heart of the sheep and of other ungulate animals. In 1906 Tawara showed that such fibres were connected with a muscular bundle which rose in the wall of the auricle the orifice of the coronary sinus and entered the ventricle along the upper border of the interventricular system [1]. In many cases of malformed heart the primitive relations of the auriculo-ventricular (a.v.) bundle may be seen (Fig. 409). It passes along the upper border

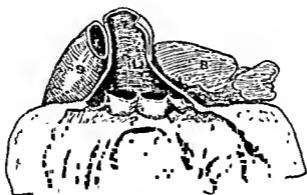


FIG. 409.

ventricle, S, interventricular septum, R, pulmonary artery.

of the interventricular septum below the interventricular foramen. Its left branch descends on the septum to the musculi papillares of the left ventricle; the right division or branch passes along the moderator band, which marks the junction of the bulbus cordis with the body of the right ventricle. When it is remembered that the ventricles arise from evaginations of the ventricular tube, it will be seen that the bundle on the upper border of the septum occupies the least disturbed part of the lumen of the primitive cardiac tube [2].

The evolution of the Purkinje system may be realized from a study of Fig. 410. Gaskell found in 1883 that the auricles and ventricles were connected in fishes, amphibians and reptiles by the musculature of the

auricular canal (Fig. 410, 4, 4), and that this connection conveyed the wave of contraction from auricle to ventricle. The auriculo-ventricular muscular collar begins in a ring of peculiar muscle cells situated as shown in Fig. 410, 3, 3. In the mammalian heart the primitive muscle of the auriculo-ventricular canal disappears—and is replaced by an outgrowth from the a.v. node. (Walls). The node in which the bundle arises represents a remnant of the ring of peculiar muscular tissue that surrounds the auriculo-ventricular junction [2]. It is true that the sinus venosus reaches the posterior endocardial cushions (Fig. 401) near

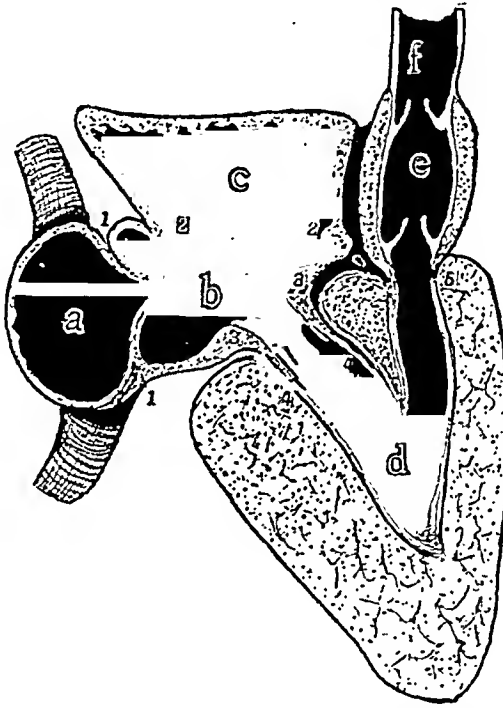


FIG. 410. Section of a Generalized Type of Heart to show the Origin of the Auriculo-ventricular Bundle and Node. *a*, sinus venosus; *b*, auricular canal; *c*, auricle; *d*, ventricle; *e*, bulbus cordis; *f*, aorta; 1, 1, sino-auricular junction; 2, 2, auricular junction with canal; 3, auricular ring of peculiar fibres; 4, auriculo-ventricular musculature; 5, bulbo-ventricular junction.

the site of the node, but it is most improbable, in the light of comparative anatomy, that the node at the commencement of the bundle should represent sinus musculature.

Changes in the Circulation at Birth.—When the umbilical cord is tied at birth the outflow of foetal blood to the placenta, by means of the umbilical arteries, and its inflow through the umbilical veins are immediately arrested. There are also other means at work that bring about the closure of these vessels. There is an immediate contraction of their muscular coats; endothelial proliferation ultimately occludes their channels [3]. At the same time the ductus venosus, which short-circuited the placental blood to the heart, is shut by the contraction of

its muscular coat, soon becoming reduced to the state of a ligament. Evidence that has been brought forward by Sir Joseph Barcroft and by those associated with him [4] has led us to see that the closure of the ductus arteriosus is not the passive mechanical process we had supposed it to be. Within 5 minutes from the time of birth the lumen of the ductus is closed by the active and tonic contraction of its muscular coat. Thus the impure blood issuing from the right ventricle by means of the pulmonary aorta can no longer pass to the descending aorta, but must enter the pulmonary circulation. This is aided by the fact that the first breath expands not only air spaces in the lungs but also the pulmonary

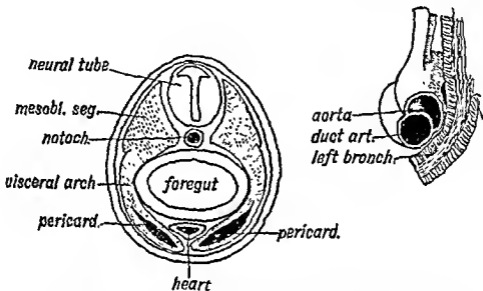


FIG. 411.

FIG. 412.

FIG. 411 Diagrammatic section across the Head Fold of a developing Salamander to show the relationship of the Pericardial part of the Coelom to the Heart and Foregut (After C. Rabl.)

FIG. 412 Section across the Junction of the Aorta and Ductus Arteriosus (viewed from behind) of a full-time Foetus to show the inflection of the Wall of the Ductus within the Lumen of the Aorta

vessels. A section of the aorta at its junction with the ductus arteriosus (Fig. 412) shows that before birth the septal wall of the ductus is invaginated within the lumen of the aorta; after birth the septal wall is bent within the lumen of the ductus, thus helping in its obliteration. The most important change of all concerns the foramen ovale. By its means the purified blood coming from the placenta passes from the right auricle to the left and so to the left ventricle, by which it is distributed to the central nervous system and to those parts of the body that lie above the sternum. With the establishment of the pulmonary circulation at birth the pressure of blood within the left auricle leads to the closure of the foramen ovale by the application of the septum ovale, which thus serves as a valve. The mechanism by which the foramen

ovale is finally obliterated has been already dealt with (p. 451). By means of the mechanisms just described the placental circulation of the foetus is converted into the pulmonary circulation of the new-born child. In the placental circulation the ventricles have equal work to do and hence their walls are of equal thickness. In the child the pressure within the aorta becomes three times that within the pulmonary artery, and hence the wall of the left ventricle becomes nearly three times as thick as that of the right [5].

Remnants of the Foetal Circulation in the Adult.—The nature of these remnants has been already described; they need only be enumerated here. They are: (i) obliterated hypogastric (umbilical) arteries; (ii) umbilicus; (iii) round ligament of the liver; (iv) fibrous remnant of the ductus venosus; (v) Eustachian valve; (vi) foramen ovale; (vii) fibrous remnant of the ductus arteriosus.

Changes in the Position of the Heart.—The alteration in the position of the heart from a subpharyngeal to a thoracic position during the 5th, 6th and 7th weeks of development is brought about by two factors. First, the heart is primarily a pump for forcing the blood through the organ of respiration; hence in the fish it lies beneath the gills, in air-breathing vertebrates it is situated close to the roots of the lungs. Secondly, in reptiles, birds and mammals a neck is developed, the head and pharyngeal region being gradually carried forwards, while the heart and pericardium come to lie opposite the middle part of the dorsal region of the spine. The neck is differentiated in the human foetus during the 2nd month. All the structures in the neck become elongated—the oesophagus, trachea, vagus nerves, jugular veins and carotid arteries. During this change the arch of the aorta and its branches are evolved from the stem or sac of the ventral aorta and from the aortic arches. In most mammals the *left carotid* arises from the base of the aortic stem (innominate artery), and a reversion to this type is the commonest abnormality to which the aortic arch is liable in man (see p. 359). The separation of the left carotid from the innominate in man is due to the large size of the upper aperture of his thorax. The left vertebral artery or the thyroidea ima may gain an origin from the aortic arch.

Final Fixation of Heart.—As may be seen from Figs. 387 and 414, the heart of the human embryo is fixed within the pericardium exactly as in a fish—being attached behind to the septum transversum by the venous mesocardium and under the pharynx by the arterial mesocardium. By the 8th week the interventricular septum is complete and the heart has taken up its position in the thorax, being fixed within the pericardium in the same manner as in the adult (Fig. 413). The original mesocardia can still be recognized separated by the transverse sinus of the peri-

cardium (Fig. 413, *b*). The transverse sinus may also be recognized between the attachments of the fish's heart (Fig. 414). The derivatives of the truncus arteriosus—the aortic root and pulmonary trunk—lie

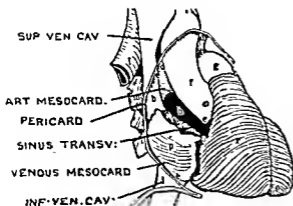


FIG. 413.

FIG. 413. The Heart pulled forwards to show its two Attachments by the Arterial (*d*, *d*) and Venous (*e*, *e*) Mesocardia.

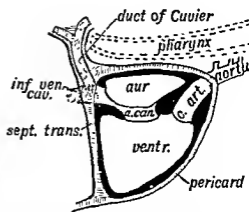


FIG. 414.

FIG. 414. Diagram of the Heart of a Fish to show. (1) the Primitive Parts of the Heart; (2) the Relationship of the Heart to the Pharynx; (3) the Septum Transversum, (4) the fixation of the Heart

within the reflections of the arterial mesocardium; the caval and pulmonary veins reach the auricles through the reflections of the venous mesocardium. That part of the septum transversum which contained

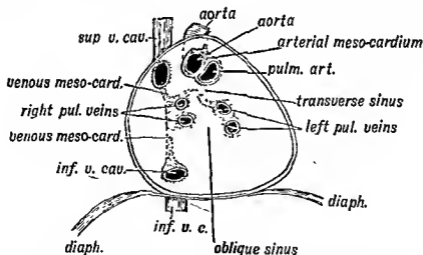


FIG. 415 View of the Interior of the Pericardium showing the Attachments of the Heart to its Dorsal Aspect by the Arterial or Venous Mesocardia

the sinus venosus and great veins has become an intrinsic part of the dorsal wall of the pericardium. The heart has so doubled on itself that the venous and arterial mesocardia are in contact, being only separated by a potential space—the transverse sinus (Fig. 415).

ovale is finally obliterated has been already dealt with (p. 451). By means of the mechanisms just described the placental circulation of the foetus is converted into the pulmonary circulation of the new-born child. In the placental circulation the ventricles have equal work to do and hence their walls are of equal thickness. In the child the pressure within the aorta becomes three times that within the pulmonary artery, and hence the wall of the left ventricle becomes nearly three times as thick as that of the right [5].

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the aorta opposite the 1st lumbar segment; by the end of the 5th week their origin has migrated backwards to the level of the last lumbar segment. In the course of their migration the umbilical arteries arise from the aorta by several roots—which simulate arches. Although the umbilical arteries appear to be direct continuations of the dorsal aortae in later embryonic and foetal life, yet there can be no doubt that this honour falls to the middle sacral artery, for, as we have seen (p. 38), the umbilical arteries must be regarded as greatly modified vesical or allantoic branches of the aorta. The middle sacral artery is formed by

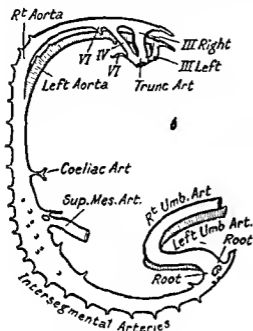


FIG. 416.

FIG.

Fig.

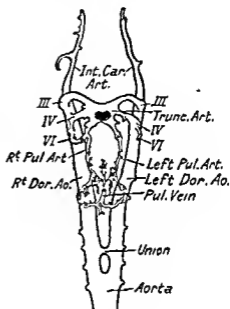


FIG. 417.

the fusion of the caudal arteries—morphological continuations of the dorsal aortae. The coeliac axis, superior and inferior mesenteric arteries are the sole survivors of the numerous branches supplied by the paired aortae to the archenteron. At the end of the 5th week the *coeliac axis* arises from the aorta opposite the 7th cervical segment; by the end of the 7th week its origin is opposite the 10th thoracic segment—its permanent position. The superior and inferior mesenteric arteries undergo a corresponding degree of migration backwards during the 6th and 7th weeks. The subclavian arteries arise at first from the dorsal aorta (Fig. 417); when the heart and aortic arches have moved backwards into the thorax, the subclavian artery remains fixed in position and thus comes to arise in connection with the 4th aortic arch.

The venous mesocardium becomes much more extensive by the ingrowth and separation of the pulmonary veins. These grow in from the lungs, and pierce the pericardium to reach the left auricle (Fig. 415). They reach the auricle through the mesentery or venous mesocardium of the sinus venosus. The migration of the left pulmonary veins causes a prolongation of the venous mesocardium to the left side; when the heart is removed the venous mesocardium is seen to be F-shaped in section. The oblique sinus lies in the concavity of the pulmonary venous mesocardium (Fig. 415).

Primitive Relationships of the Pericardium.—Were one to restore the head and pericardium to the relative positions they occupy in the 5th week of development, then the pericardium must be lifted from the thorax and placed beneath the chin and larynx so that the septum transversum is opposite the origin of the phrenic nerve from the 4th cervical segment; the anterior border of the umbilicus is also then opposite the origin of the phrenic nerve. In the somatopleure over the pericardium and between the mandible and umbilicus are developed the depressors of the hyoid, the sternum and sternal ribs. The pericardium is therefore the coelom of the neck; its fibrous wall represents the deepest layer of the cervical somatopleure, corresponding to the fascia transversalis of the abdomen. With the elongation of the neck and separation of the pharynx and pericardium, the tissue of the branchial segments which surrounds the aortic arches is drawn out to form the carotid sheaths.

Ectopia Cordis.—Occasionally children are born with their hearts exposed on the surface of the chest. In extreme cases only the dorsal wall of the pericardium is present, and it is flush and continuous with the skin of the chest. In these cases the sternum is partially absent, or if present it is cleft, the right and left halves being widely parted. No satisfactory embryological explanation of this condition has yet been given [6].

Dorsal Aortae [7].—The dorsal or descending aorta, like the heart, is bilateral in origin. At the beginning of the 4th week, as somites are being demarcated in the cervical region of the embryonic plate, the right and left dorsal aortae, commencing at the upper ends of the pharyngeal arches, pass backwards side by side, supplying branches to the arch-enteron as they go (Fig. 291). The dorsal aortae arise by the union of endothelial-lined spaces and are at first simple endothelial channels. From their terminal branches on the yolk sac commence the umbilical arteries (Fig. 29). By the end of the 4th week the dorsal aortae have fused to form one vessel from the 1st thoracic to the 1st lumbar segment (Fig. 417). At this date the radicles of the *umbilical arteries* arise from

until the end of the 6th. After this date centres of blood formation, factories, are set up in the mesenchymal tissues of the liver, which remain the chief centres of production until the 6th month of foetal life. At the same time the tissues of the spleen also provide shelter for blood brooding. Late in the 3rd month blood factories begin to be established in the cancellous spaces of bones; ultimately bone marrow becomes the chief source of new blood corpuscles, both red and white. Whether the factories in the liver and spleen were set up by colonists from the yolk sac or are established by powers resident in the local mesenchyme of these organs is still open to debate, but the balance of evidence favours local development. The same uncertainty prevails regarding the origin of blood centres in bone marrow.

Lineage of Blood Corpuscles [11].—We now turn to the origin and

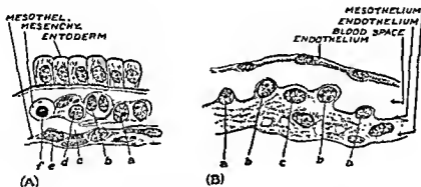


FIG. 418.

- A. Section of the Wall of the Yolk Sac to show the constitution of a Blood Island. (H. E. Jordan) a, Haemoblast, dividing; b, Erythroblast, dividing; c, Blood-space; d, Haemoblast; e, Endothelial Cell; f, Leucoblast.
- B. Wall of Blood-space, showing Blood Cells arising from its Endothelium. (H. E. Jordan) a Endothelial Cell; b, Haemoblast being produced from Endothelial Cell; c, Haemoblast arising outside Blood-space from Endothelium.

lineage of the various kinds of corpuscles found in the circulating blood. In Fig. 419, A, a section of the wall of the yolk sac is depicted. Between its inner lining of endoderm and its outer endothelial (serous) coat there is a stratum of mesenchymal cells, some of which are being differentiated into primitive blood cells (haemoblasts or haemocytohlasts), others into enclosing endothelial (vasoformative) cells. Blood and its vascular walls arise from cells apparently alike in structure and origin. In Fig. 418, A, is seen an island of haemoblasts, still unenclosed by endothelial cells. This island is a centre of erythroblast production; it is the rule in the yolk sac for new cells to be formed within a vascular wall; in the liver and marrow, formation is chiefly extra-vascular. No sharp line can be drawn in the wall of the yolk sac between endothelial cells and haemoblasts; in Fig. 418, B, endothelial cells are shown in the process of becoming haemoblasts.

Formation of Blood Vessels [8].—The largest artery or vein of the body begins as a simple capillary. The manner in which capillaries are transformed into arteries and veins can be well observed in the mesenchymal tissue of a developing limb bud. The somatic capillaries at the base of the bud send out invading processes, at first solid, but soon canaliculized. These vascular processes unite within the limb bud so as to form a tier of arches. From these primary arches new processes grow out to form secondary and then tertiary tiers, and thus the limb bud becomes permeated by a plexus of capillaries. Some of the capillary channels serve for the inflow of blood; others for its outflow. Certain of the inflow channels enlarge, while their neighbours are absorbed. In this way main arterial vessels arise, being provided with muscular and other coats by adjoining mesenchymal cells. Fibroblasts can be converted into muscle cells. Venous channels are established in a similar manner. Thus the axillary artery and vein are, in reality, greatly modified capillaries.

Especially instructive are the observations made by E. and E. Clark on the development of vessels within transparent chambers set within the ears of living rabbits [9]. Into the coagulum within the chamber, after the lapse of 36–48 hours, proceed invading capillary processes; these form loops and arches as in the developing limb bud of an embryo. If the flow of blood becomes rapid, communications are formed between adjacent inflow and outflow channels, arterio-venous anastomoses being thus formed.

Formation of Blood.—In the development of each system of the human body the various parts appear in the same order as they are seen to occur in ascending the scale of the animal kingdom. In many invertebrate animals the blood is made up of only a fluid element, the *plasma*. When the human heart first beats, its lumen contains no blood cells, only plasma. In amphioxus nucleated uncoloured cells appear in the plasma. In all other vertebrates nucleated red, as well as nucleated white, cells are constituent elements of the blood. Haemoglobin-carrying nucleated cells (erythroblasts) begin to appear in the foetal circulation late in the 6th week; white nucleated cells (leucocytes) make an appearance about a week later. Although the final form of red cell, the denucleated erythroblast (erythrocyte) begins to be formed towards the end of the 2nd month, the nucleated type is still being formed, and circulates, until a few days after birth. Thereafter, in normal health, only definite erythrocytes are in circulation.

The observations of Bloom and Bartlemez [10] seem to have established that, so far as the human embryo is concerned, the wall of the yolk sac is the first and only source of blood cells from the end of the 3rd week

By the end of the 3rd month lymphoblasts are found in connective tissues of various regions of the foetal body, usually in the proximity of lymphatic vessels. They also become assembled in vast colonies or nodes. The lifetime of a lymphocyte appears to be very brief; Prof. Yoffey [13] has estimated that the whole lymphocyte population is replaced twice daily, such a turnover entailing an extreme rapidity of reproduction. Lymphocytes are a product of the lymphatic system and hence are not produced in marrow, which is devoid of this system. Lymphocytes found in marrow have escaped from the circulation [14]. Monocytes, although resembling lymphocytes in appearance, are of a different nature functionally and morphologically [15].

Lymphatic System [16].—In all vertebrate animals the plasma or lymph from the tissues of the body is drained into the veins by a special

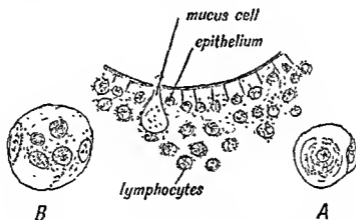


FIG. 419 Section of a tubular part of the Thymus of a Frog, showing (1) the supposed

system—the lymphatic vessels. In fishes they may contain red blood, being derived apparently from veins [17]. In amphibia the lymph collects in large spaces lined by endothelium, from which it is forced into the venous system by two pairs of lymph hearts—one pair situated in the angle between the jugular and subclavian veins, the other pair between the internal and external iliac veins. In mammals the lymph hearts disappear; they are no longer required, for the negative pressure in the veins of the thorax, set up by the evolution of a separate respiratory cavity, is sufficient to draw the lymph into the venous system. It is remarkable, however, that Prof. Florence Sahin, who by a paper published in 1902 inaugurated a knowledge of the development of the mammalian lymphatic system, found that the lymph vessels appear first at those four points where the amphibian lymph hearts are situated.

Of the four great races into which the cellular elements of the blood may be divided—erythrocytes, granulocytes, lymphocytes and monocytes—the chief two, the erythrocytes and granulocytes, have a closely linked lineage. Both spring from a common ancestral type of haemoblast represented by a common type in the yolk sac, in the liver and, later, in red bone marrow. This common ancestral haemoblast has its representative type in the myeloblast of the marrow. Lymphocytes, although they do not appear in the embryonic circulation until the 7th week, are, so far as their origin is concerned, collaterals of the haemoblasts; they are the progeny of endothelial cells lining vascular channels. It is a remarkable fact that the haemoblasts that are developed first in the wall of the yolk sac are always described as large lymphoid cells. The remaining race of blood constituents, the monocytes and allied cells, are of still older lineage, for they retain powers inherent in embryonic mesenchyme.

Tracing the lineage of red corpuscles (erythrocytes) is complicated by two factors. The first of these occurs in the yolk sac, where until the end of the 2nd month two kinds of “reds” are being produced, a large and temporary form, the progeny of large primitive haemoblasts, and the smaller and permanent type, produced by normal haemoblasts. The second complicating circumstance affects the production of reds at all stages of life. Erythrocytes may reach their final form by passing through two, or perhaps three, differing developmental stages [12]. Granulocytes too, although they arise from the same parental haemoblast (myeloblast), become differentiated into three forms or kinds, neutrophils, eosinophils and basophils. An embryo's blood group is fixed by the end of the 2nd month.

The Origin of Lymphocytes.—The reticular tissue that underlies the epithelial lining of the alimentary canal corresponds to the blood-forming stratum of the yolk sac. From the 3rd month onwards the submucous coat of the alimentary tract is a seat of lymphocyte production. We have already seen how endodermal outgrowths from the pharyngeal end of the tract become sites of lymphocyte proliferation (p. 373). The drawing reproduced in Fig. 419 was intended to demonstrate, in the frog, a direct transformation of endodermal cells into lymphocytes. The more probable explanation is that the endodermal cells of such bodies as the tonsil and thymus attract and provide pabulum for the proliferation of circulating lymphocytes. I must also set down here a fact which is against a view expressed in a preceding paragraph, namely, that lymphocytes and granulocytes are of different lineage and nature. Against this must be set the fact that Bloom succeeded in transforming lymphocytes into granulocytes by growing them in a cultural medium.

side of the neck spread and invade the tissues of the neck, head and arm—all save the central nervous system and voluntary muscles. These are not drained by the lymphatic system. The great lymph sacs are

jugular vein, the orifice being guarded by valvular folds.

Another pair of lymph sacs appear in the pelvis—related to the corresponding iliac veins, into which they at first open (Fig. 420). From the pelvic or iliac sacs outgrowths invade the hind limbs and tissues of the pelvis and buttocks. In the mesenchymal tissue in which the dorsal aorta is embedded there appear a series of endothelial-lined lymphatic spaces, which become united and place the posterior or iliac sacs in communication with the jugular sacs. In this way two thoracic ducts are formed at the end of the second month. Two other retroperitoneal centres appear, one at the root of the superior mesenteric artery, from which arises the system of vessels which drains the alimentary tract; the other, to give

system is just as much a vascular system as is the venous system; everywhere its walls are lined with endothelium. Nowhere does it communicate with "tissue spaces."

The investigations of E. and E. Clark [20] have demonstrated that in normal tissue, whether embryological or fully developed, there are no "spaces"; everywhere cells and fibres are embedded in a gel. The lymphatic spaces of amphibia are enormously dilated lymph vessels.

Lymphatic Nodes.—These make their first appearance at the end of the 3rd month of development, being formed at the sites of lymph sacs and along leashes of lymphatic vessels leading to these sacs [21]. They appear first as follicles which are developed within the lumina of vessels; thus the lymph passing along these channels is exposed to the lymphocytes developed in the reticular tissue of the follicle. Later a localized plexus of lymphatic capillaries is formed; the plexus is invaded by lymphocytes that are aggregated so as to form lymphoid nodules. The nodules are invaded by blood-vessels, their substance becoming differentiated into cortex and medulla. Such are the stages in the development of lymphatic nodes. Lymphocytes arise within the nodes by the proliferation of the endothelial cells that line their lymphatic vessels and spaces. The lymphatic nodes grow in size and in number during each month of foetal life, serving as germinal centres for the production of lymphocytes.

Interscapular Body.—Under this name has been included the mass of peculiar tissue which occupies the posterior triangle of the neck and

Enquiries by American embryologists, especially by Huntington and McClure [18], threw quite a new light on the origin of the lymphatic system. They established that the formation of lymph vessels begins at definite centres and from such a centre vessels spread outwards, vascularize and drain a definite area. If the starting centre is excised, then there is no outgrowth and vessels from neighbouring areas invade and drain the one thus deprived. While the angioblasts of the blood

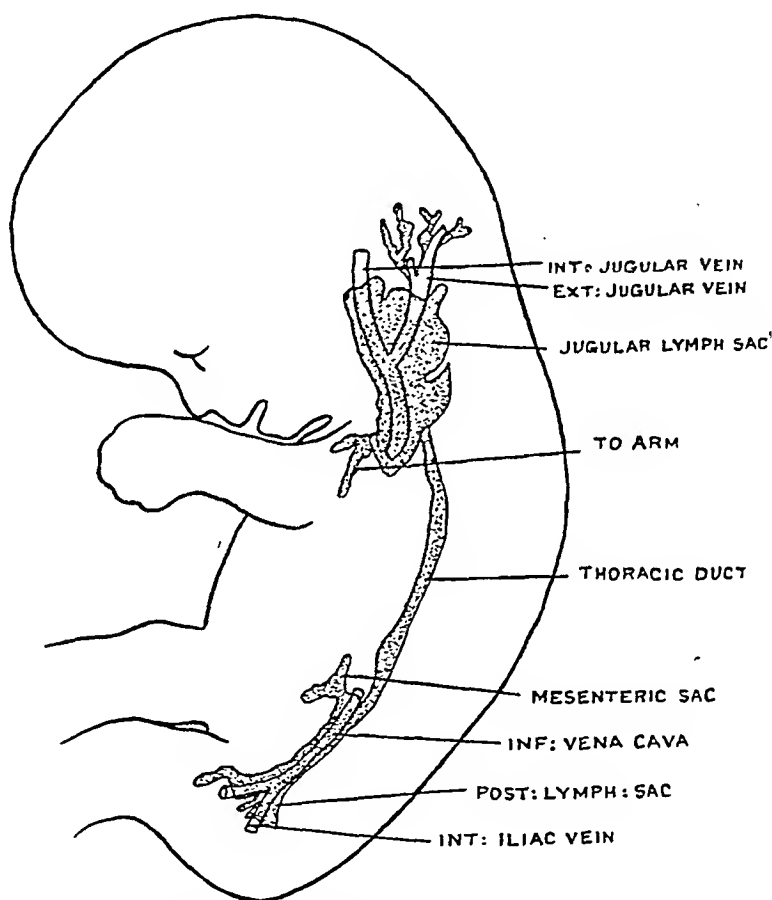


FIG. 420. The Main Lymphatic Vessels and Sinuses of the Human Foetus at the beginning of the 3rd month. (After Prof. Florence Sabin.)

system are everywhere and have established a complete vascularization of the embryonic tissues before the end of the 4th week, the angioblasts of the lymphatic system do not become manifest until the end of the 6th week, when they form a capillary network in the centres of initiation. The greatest and earliest centre is situated in the angle between the jugular and subclavian veins, where the termination of the thoracic duct is afterwards formed. By the end of the 8th week the capillary network of lymph vessels has fused and formed the extensive lymph sac shown in Fig. 420. In the 3rd month outgrowths from the jugular sac on each

side of the neck spread and invade the tissues of the neck, head and arm—all save the central nervous system and voluntary muscles. These are not drained by the lymphatic system. The great lymph sacs are merely temporary structures; their cavities are filled by reticular lymphoid tissue produced by the lymphatic endothelium which lines the sacs. As soon as formed, the jugular lymph sac effects a union with the jugular vein, the orifice being guarded by valvular folds.

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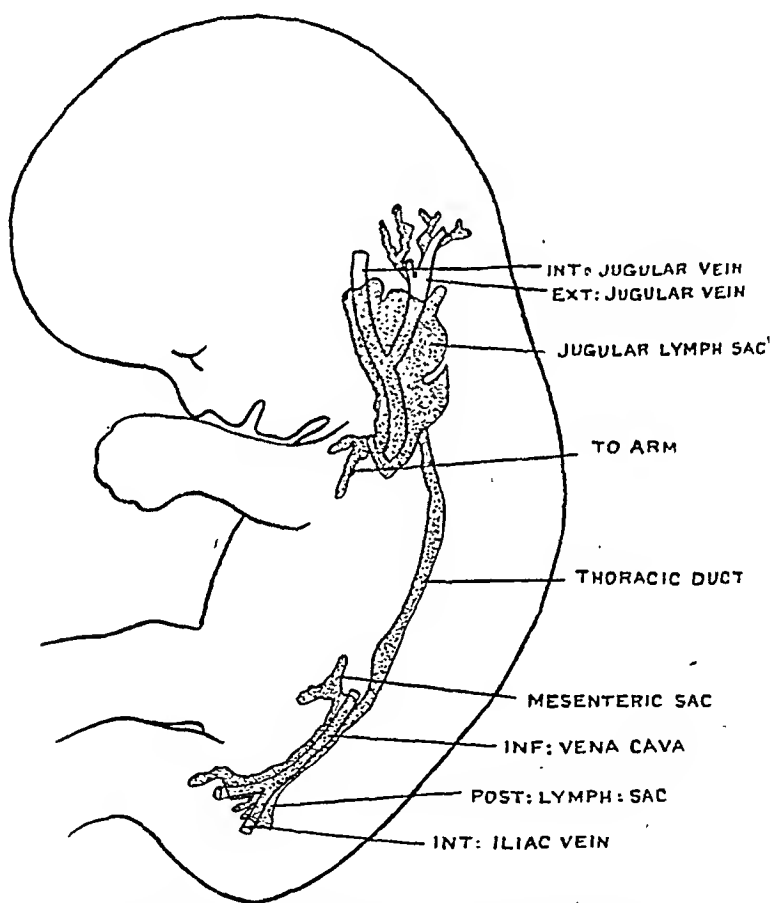


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[7] Jackson, J. L., *Amer. Jour. Anat.*, 1935, 56, 305 (development of the dorsal aortae).

[8] For recent papers on the development of blood-vessels, see: Woodlard and Harpman, *Jour. Anat.*, 1938, 72, 18; Hughes, F. F. W., *ibid.*, 1936, 70, 76; 1938, 72, 1; Goldner, J., *Ann. d'Anat. Path.*, 1934, 11, 401. Especially noteworthy are the observations made by Eliot and Eleanor Clark on the development of blood-vessels seen within their transparent "ear chambers": see *Amer. Jour. Anat.*, 1934, 55, 47; *ibid.*, p. 407 (formation of arterio-venous communications); *ibid.*, 1935, 57, 385; 1939, 64, 251; 1940, 66, 1; Szepeswol, J., *Archiv. d'Anat.*, 1932, 15, 47; Spanner, R., *Zeitsch. Anat. Entwickl.*, 1937, 107, 124; Stalkunow, S., *ibid.*, 1937, 106, 20 (describes a cambium layer under the intima of arteries which adds to the media on the one side and to the endothelium on the other). For vascularization of the foetal scalp, see Finley, Ellen B., *Contrib. Emb.*, 1922, 14, 165.

[9] For recent accounts of development and lineage of blood corpuscles, see: Bloom and Bartlemez, *Amer. Jour. Anat.*, 1940, 67, 21; Gilmore, J. R., *Jour. Path. Bact.*, 1941, 52, 25; Israels, M. G. G., *Lancet*, 1941, 2, 207; Jordan, H. E., *Quart. Rev. Biol.*, 1933, 8, 58; *Amer. Jour. Anat.*, 1932, 51, 215; *ibid.*, 1935, 57, 1; Michels, N. A., *ibid.*, 1935, 57, 439; Wintrobe and Shumacker, *ibid.*, 1936, 58, 313; Slonimski, P., *Anat. Anz.*, 1938, 85, 55 (suppl.); Duthie, E. S., *Jour. Anat.*, 1939, 73, 396 (in teleosts). The following papers deal with the origin of the various forms of white corpuscles: Levi, G., *Ergeb. Anat. Entwickl.*, 1934, 31, 125; Clark, E. and E., *Amer. Jour. Anat.*, 1936, 69, 12; *Anat. Rec.*, 1937, 68, 237; Jordan and Bloom, W., *Anat. Rec.*, 1937, 69, 99; Geweb., 1931, 11, 249 (origin of granulocytes); Gray, J. H., *Jour. Anat.*, 1935, 69, 153 (mast-cells).

[10] Bloom and Bartlemez, see preceding note.

[11] See references given in note [9].

[12] See references given in note [9].

[13] Yoffey, J. M., *Jour. Anat.*, 1936, 70, 507 (renewal of lymphocytes); Drinker and Yoffey, *Lymphatics, Lymph and Lymphoid Tissue*, 1941.

[14] Yoffey and Parnell, *Jour. Anat.*, 1944, 78, 100.

[15] Lewis, W. H., *Anat. Rec.*, 1938, 70, 51 (suppl. 3).

[16] For development of lymphatic vessels, see: Sabin, Florence, *Amer. Jour. Anat.*, 1902, 1, 367; *ibid.*, 1909, 9, 53; Clark, E. and E., *ibid.*, 1933, 52, 273; 1936, 60, 253; 1938, 62, 59; Gray, J. H., *Jour. Anat.*, 1938, 72, 622; 1940, 74, 309 (regeneration of lymphatics); Harris, H. A., *Brit. Med. Jour.*, 1937, 1, 166; Webb, R. L., *Anat. Rec.*, 1933, 57, 348 (contractility of walls).

[17] Burne, R. H., *Phil. Trans.*, 1929, 217 (B), 335; Cole, F. J., *Trans. Roy. Soc. Edm.*, 1925, 54, 309.

[18] *Amer. Jour. Anat.*, 1910, 10, 177.

[19] Lewis, W. H., *Johns Hopkins Hosp. Bull.*, 1931, 48, 243; Kampmeier, O. F., *Amer. Jour. Anat.*, 1928, 46, 413; Shore, L. R., *Jour. Anat.*, 1928, 62, 125 (lymphatics of heart).

[20] Clark, E. and E., see references in note [16].

[21] For recent papers on the origin of lymphatic nodes, see: Conway, E. A., *Anat. Rec.*, 1937, 69, 487; Dabelow, *Anat. Anz.*, 1936, 81, 187 (suppl.); Lewis, W. H., *Anat. Rec.*, 1938, 70, 51 (suppl. 3); Hummel, K. P., *Amer. Jour. Anat.*, 1935, 57, 351 (lymphoid follicles); Kindred, J. E., *ibid.*, 1938, 62, 453 (structure of node).

[22] Inglis, K., *Jour. Anat.*, 1927, 61, 452.

[23] Jordan, H. E., *Anat. Rec.*, 1934, 59, 461.

[24] Jordan, H. E., *Anat. Rec.*, 1934, 59, 297; Selye and Schenker, *Jour. Anat.*, 1939, 73, 413.

extends under the trapezius towards the posterior border of the scapula [22]. It represents the *hibernating gland* of insectivora and bats. It begins to form in the 2nd month of foetal life at the site of the jugular lymph sac. It is composed of a stratum containing three tissues—lymphoid, haemolymph (blood-forming) and granular cells which contain scattered droplets of fat. Prof. Jordan has drawn attention to the transformation of fatty tissues in various regions of the body of the foetus into blood-forming centres [23].

Haemolymph Nodes [24].—In the subperitoneal fat of many mammals numerous red bodies may be seen which differ from lymphatic glands in the following points: (i) the sinuses contain red blood corpuscles; (ii) instead of afferent and efferent lymphatic vessels, arteries and veins open into the sinuses. They occur in the human foetus, and apparently serve the same function as the spleen.

Bone Marrow.—Until the 4th month of foetal life the marrow is composed of branching cells embedded in a jelly-like matrix (primary marrow); it then assumes the appearance of lymphoid tissue, and contains leucoblasts; in the 6th month erythroblasts and erythrocytes appear in the dilated capillaries, forming *red marrow* in the centres of ossification (Hammar). At birth the marrow of all the osseous tissue is red; during the years of active growth the marrow of the shafts of bones is gradually replaced by fat cells, *yellow marrow* being thus formed. From birth onwards the red marrow forms the only tissue in which red blood corpuscles are produced.

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[2] For later literature on the a.v. conducting system, see Davies, F., *Jour. Anat.*, 1931, 65, 339 (Monotreme heart); *ibid.*, 1930, 64, 129, 319 (bird's heart); Shaner, R. F., *Anat. Rec.*, 1929, 44, 85 (calf's heart); Blair and Davies, *Jour. Anat.*, 1935, 69, 305; Davies and Francis, *Phil. Trans.*, 1941, 231 (B), 99; Adams, W. E., *Proc. Zool. Soc. Lond.*, 1937, B, 417 (bird's heart); Rondolini, G., *Zeitsch. Anat. Entwickl.*, 1937, 106, 782; Abramson and Margolin, *Jour. Anat.*, 1936, 70, 250; Walls, E. W., *ibid.*, 1945, 79, 45; *ibid.*, 1947, 81, 93.

[3] Meyer, A. W., *Amer. Jour. Anat.*, 1914, 16, 477.

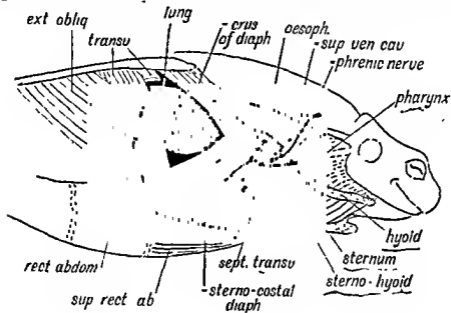
[4] For changes in circulatory structures at birth, see: Barcroft, Sir J., *Researches on Pre-Natal Life.*, 1947; Franklin, Barclay and Prichard, *Jour. Anat.*, 1941, 75, 75 (in foetal lamb); Barclay, Barcroft and Others, *Amer. Jour. Anat.*, 1942, 69, 363; *Brit. Jour. Radiol.*, 1938, 11, 570. For closure and structure of ductus arteriosus, Boyd, J. D., *Jour. Anat.*, 1938, 72, 146; 1941, 75, 457 (nerve mechanism); Noback and Rehman, *Anat. Rec.*, 1941, 81, 505; Kennedy and Clark, *ibid.*, 1941, 79, 349; Hayek, H. von, *Zeitsch. Anat. Entwickl.*, 1936, 105, 15.

[5] Keen, J. A., *Jour. Anat.*, 1945, 79, 38.

[6] See report of a case by Dr. J. Ledényi, *Anat. Anz.*, 1935, 79, 277.

centre—both motor and sensory—in the hind-brain, and visceral nerves supplied by the vagus, and from vasomotor centres in the dorsal region of the cord. Although branchiae are never developed in the human embryo, yet the condition in the 4th and 5th weeks, when the heart is subpharyngeal in position and the visceral and aortic arches are in process of development, can only be explained by the supposition that at one stage of evolution these parts had served a respiratory purpose.

Stage II.—In most amphibians four parts are to be recognized in the respiratory system. (i) The swim bladder is bifid; each half, now properly called a lung [1], projects within the abdominal cavity above the pericardium and liver (Fig. 423). (ii) A respiratory passage leading



FIG

from the pharynx to the lungs, and formed from the 2nd, 3rd and 4th branchial (4th, 5th and 6th visceral) arches. (iii) The vascular system for each lung rises from the artery of the 6th visceral arch (Fig. 417). (iv) The branchial muscles, which formerly forced water through the gill slits, are now transmuted into pharyngeal muscles and help to pump air into the lungs—thus acting as muscles of inspiration. The muscles of the body-wall (see Fig. 423) are modified to form the muscles of expiration. Two parts of these are specially worthy of notice, because in mammals they become the diaphragm: viz. (a) part of the transversalis sheet, which rises from the spine and ends in the pericardium, oesophagus and roots of the lung; (b) a deep lamina of the rectus

CHAPTER XXIV

RESPIRATORY SYSTEM

Stages in the Evolution of the Human Respiratory System.—The development of the lungs, the pleural cavities and chest wall forms one of the most complicated chapters of human embryology. The steps in the development of this system, as seen within the human embryo, are unintelligible until they are interpreted by a study of comparative anatomy, especially of those animal forms that show the manner in which a purely pulmonary system arose from one that was purely

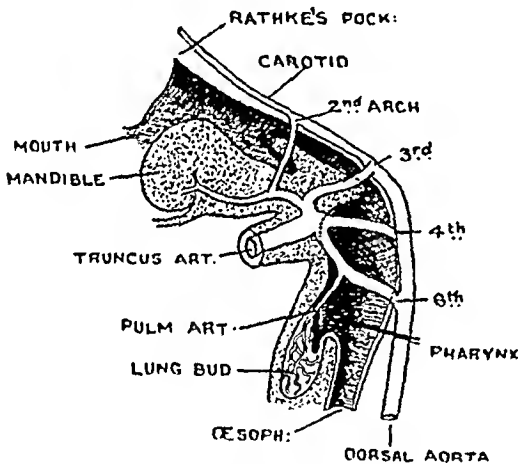


FIG. 421.

FIG. 421. Showing the Pulmonary Artery arising from the 6th Aortic Arch in a Human Embryo of 5 weeks. (After His.)

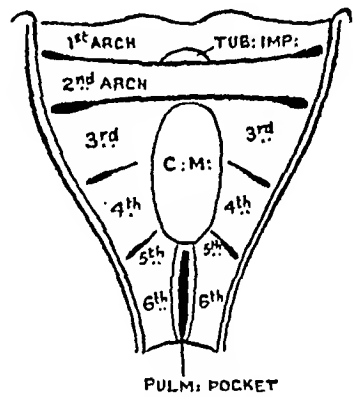


FIG. 422.

FIG. 422. Showing that the Pulmonary Diverticulum arises between and behind the bases of the last or 6th pair of Visceral Arches. (Frazer.) C.M., hypobranchial eminence.

branchial. Hence it is necessary to recapitulate briefly the various modifications of the respiratory system which are seen to occur in ascending from the lowest to the highest class of vertebrates. Four stages may be recognized :

Stage I.—This stage is represented in fishes, in which the respiratory system is made up of the following parts : (i) Branchiae, in which the respiratory exchange of blood gases is effected ; (ii) the swim bladder, an evagination from the oesophagus, containing oxygen, and surrounded by lymphoid tissue ; (iii) the musculature of the branchial arches and pharynx, which pumps water through the branchial clefts, and helps to force the blood through the branchiae ; (iv) nerve system with

The development of the diaphragm gave mammals two advantages : (i) an enormous increase in the power of inspiration ; (ii) the respiratory negative pressure, which affects all the viscera within the body cavity in reptiles, became restricted to the thorax in mammals.

Morphological Parts of the Respiratory System are : (a) The respiratory passage, which extends from the pharynx to the bronchioles of the lung. The tissues that surround this passage are derived from the coverings

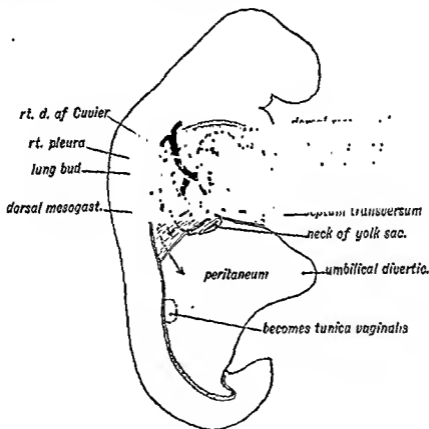


FIG. 421.

and substance of the 4th, 5th and especially the 6th arch. The nasal cavities continue the breath passages to the nostrils. We have seen how these cavities are shut off from the mouth in the latter part of the 2nd month. (b) The pulmonary tissue made up of (i) a diverticulum from the fore-gut, which represents the swim bladder; (ii) a vascular network derived from the capillaries of the fore-gut, into which opens a blood supply from the last (6th) pair of aortic arches (Fig. 421). (c) The respiratory muscles, sternum and ribs are formed in the somatopleure of the body-wall.

abdominis, which ends in the pericardium (Fig. 423, sterno-costal). The nerve to these muscular segments descends on the outer aspect of the superior vena cava exactly in the same manner as the phrenic nerve descends to the diaphragm (Fig. 423).

Stage III.—(i) In reptiles the lungs are abdominal in position, but they are no longer simple sacs; an elaborate series of compartments, separated by partitions, have appeared within the lung, thus exposing a larger vascular surface to the inspired air. (ii) The respiratory passage is elongated and demarcated into larynx, trachea and bronchi. (iii) Ribs and sternum are developed, so that the musculature of the body-wall becomes differentiated into inspiratory and expiratory muscles.

Stage IV.—In mammals an extraordinary developmental change occurs that leads to the formation of two pleural cavities and their complete separation from the abdomen by a diaphragm. The origin of the diaphragm must be sought for not in the reptiles, present or past, but in a very low form of amphibian. To understand the origin of the pleural cavities and diaphragm of mammals the following points must be kept in mind: (i) That the septum transversum, in its fully developed condition, as seen in the frog, is the fibrous layer of tissue that separates the heart from the liver; a corresponding structure is seen in the human embryo. (ii) Into the septum transversum are inserted the deepest layer of the rectus abdominis and vertebral fibres of the transversalis (Fig. 423). (iii) The ribs are developed in the two intermediate layers of the body-wall—namely, those represented by the external and internal oblique muscles [2]. The muscular fasciculi that end in the septum transversum are deep to the ribs and intercostal musculature. (iv) The lung buds lie at first in the mesentery of the fore-gut, from which they grow outwards on each side into a narrow (pleural) passage of the coelom, which leads from the pericardium to the peritoneal cavity (Fig. 424). The passage is situated at the upper border of the septum transversum; its pericardial opening, the iter venosum, is shut by the fold in which the superior vena cava is enclosed. Now, when the lung buds grow out in the mammalian embryo, they fill these passages and their hinder ends project into the abdominal cavity. Then in the 6th and 7th weeks the coelomic passage undergoes an extremely rapid expansion, growing into the body-wall so as to separate the pericardium and the deeper or diaphragmatic layer of musculature from the outer or intercostal stratum. Lung growth follows closely on expansion of the pleural cavities, which are in reality new chambers or spaces produced by an enormous expansion of the narrow coelomic or pleural passages of the embryo. We shall see (p. 482) that the septum transversum is also cleft during the expansion.

5th and 6th weeks is illustrated by Figs. 324, 325, 425, 426. In the 4th week the lung bud is a mere diverticulum; in the 5th the trachea and

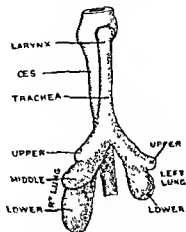


FIG. 425.

FIG. 425. The Trachea, Bronchi and Lung Buds late in the 5th week of development. (After Broman)

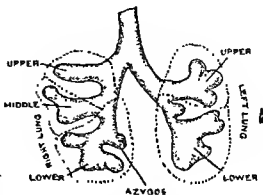


FIG. 426.

FIG. 426. The Lobulation of the Lungs in the 6th week. (After Merkel.)

buds of the main bronchi are apparent; in the 6th week the secondary bronchi and separate lobes are in process of differentiation.

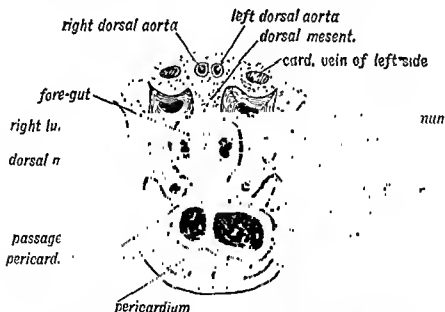


FIG. 427. A Section of a Human Embryo to show the relationships of the Pulmonary Buds at the 5th week, looking backwards. (After Kollmann)

In Fig. 427 the relationship of the lung buds is shown to surrounding structures during the 5th week. The following points should be noted :
(1) As the lung buds grow out they push their way into the pleural

Development of the Pulmonary System.—Towards the end of the 4th week, a deep median groove appears in the floor of the fore-gut, extending anteriorly to the space between the 4th pair of arches (Fig. 422). On each side of the median groove is the 6th pair of arches, sometimes called the pulmonary arches, because the pulmonary arteries are derived from their vessels. Externally the pulmonary groove appears as a sac-like swelling or diverticulum on the ventral aspect of the pharynx and oesophagus (Fig. 421). Before the end of the 5th week the opening into the pulmonary pocket has assumed the form shown in Fig. 422. It is now a linear opening, bounded on each side by a fold, the primitive laryngeal folds. The anterior end of the opening abuts on the hypobranchial eminence (Fig. 422, *C.M.*), from which the epiglottis will be formed. The primitive laryngeal aperture represents only the anterior part of the original pulmonary groove, for as we have seen (p. 382) the posterior part becomes closed by the union of its lips, thus cutting the lung bud off from the oesophagus, the separation proceeding from behind forwards. The hinder part of the diverticulum becomes the lung bud; the intermediate, the trachea; the anterior, the larynx.

Two points should be noted in the relationship of the oesophagus at the 4th week: (i) like that of a fish, it is extremely short; (ii) it lies between the right and left cavities of the coelom in the dorsal attachment of the mesocardium of the sinus venosus (Fig. 427). (iii) The part of the coelom that lies at each side of the oesophagus is the narrow passage connecting the pericardial and peritoneal cavities which becomes expanded to form the pleura.

When the pulmonary outgrowth is viewed from the side, its posterior extremity is seen to end in a deep pocket, the *pulmonary pocket* or diverticulum (Figs. 324, 429). The wall of the pocket is lined by a mass of endoderm, which ultimately forms the epithelial lining of the whole respiratory tract, from the ciliated epithelium of the trachea to the pavement epithelium lining the alveoli of the lungs [4]. Round the pulmonary bud is grouped a mass of mesodermal tissue out of which the connective-tissue system of the trachea, bronchi and lungs is developed.

In the 5th week the pulmonary pocket produces a larger right and a smaller left process, the right and left *lung buds* (Fig. 425). The right bud forms the right lung and bronchus; the left, the left lung and bronchus. As the pleural cavities and their contained lung buds develop the oesophagus elongates and a general growth movement carries the stomach and septum transversum backwards. The tracheal part of the bud becomes separated from the oesophagus, but both retain the same nerve supply—the recurrent branch of the vagus—which is part of the nerve of the 6th arch. The rapid development of the lung during the

Formation of the Bronchi and Lungs.—The bronchi are the stalks of the right and left lung buds. The right bud is the bigger; the left is probably repressed by the heart turning to the left side. This, like the persistence of the aortic arch on the left, the torsion of stomach and bowel, is part of the natural asymmetry of the mammalian body. The right lung shows three secondary buds—the forerunners of the upper, middle and lower lobes of the lung; the left, two, which form the upper and lower lobes (Fig. 425).

The condition of the lung buds during the 6th week is shown in Figs. 426, 433. Not only are the right and left bronchi formed, but so also are the chief bronchial ramifications. The terminal buds form the

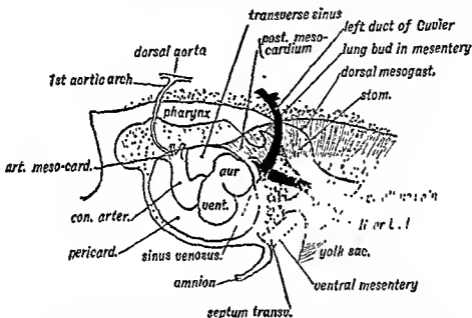


FIG 426. Diagram to show the manner in which the Heart is fixed within the Pericardium by the Arterial and Venous Mesocardia in a Human Embryo of 4 weeks. The "post mesocardium" in the above figure forms part of the venous meso-cardium

bronchioles and infundibula. Each ramification ends in a bud, which divides again and again and keeps on budding and rebudding until the 7th year after birth. Prof. Broman has estimated that the terminal infundibula of the lung at birth represent the 18th in a series of dichotomies. Each bud is solid, and carries its sheath of mesoderm; the appearance on microscopic examination is very similar to that of a gland, such as the pancreas or parotid. In the 3rd month the mesoderm or mesenchyme between the pulmonary buds is extremely abundant; by the 6th month it forms merely a thin stroma amongst the alveolar air sacs. At the 6th month saccular evaginations occur from the infundibula; they form the air cells, or alveoli. At the same time the

passages—the narrow communications between the pericardium and peritoneum. These parts of the coelom form the *pleurae*. The part of the coelomic lining that is invaginated as a covering on the lung bud becomes the visceral pleura. The invaginating or ensheathing lining of the passage becomes the parietal pleura. As the lung buds grow, they distend the originally small pleural parts of the coelom until, at the time of birth, the right and left pleurae almost meet in front of the heart and completely separate the chest wall from the pericardium and diaphragm (Fig. 444). They meet after birth under the sternum, enclosing between them the anterior mediastinum.

(ii) As will be seen from Fig. 424, the lung buds sprout out from the

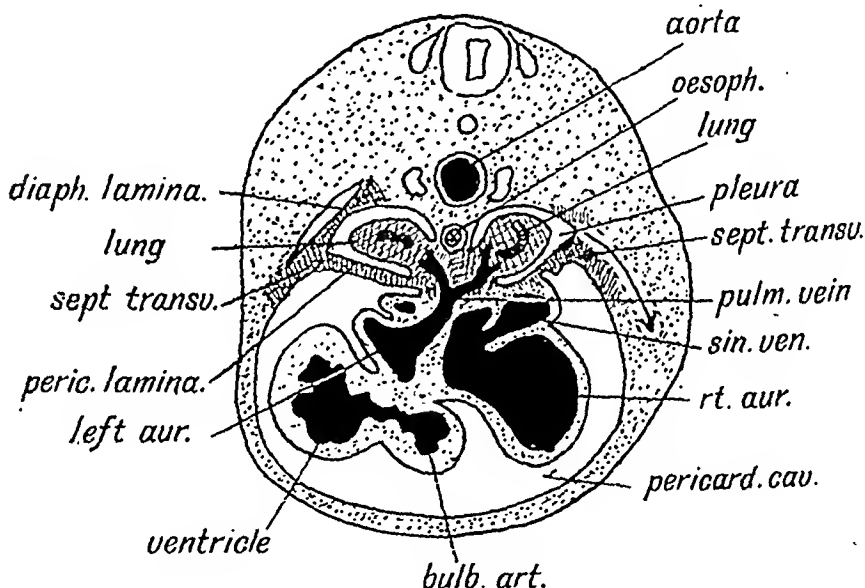


FIG. 428. Transverse section of a Human Embryo showing: (1) the Outgrowth of the Lung Buds from the Mesentery of the Fore-gut; (2) the Separation of the Pericardium from the Body-Wall and Formation of the Pleural Cavities; (3) the Separation of the Diaphragmatic Lamina from the Septum Transversum. The arrow shows the direction in which the right pleura invades the body-wall. (After Lockwood.)

mesentery just behind the duct of Cuvier. This relationship is retained in the adult, the vena azygos major and superior vena cava lying above and in front of the root of the right lung. The roots of the lungs represent the situation at which the embryonic pulmonary outgrowth took place. If the left duct of Cuvier persisted it would lie above and in front of the root of the left lung. The ductus arteriosus—part of the 6th arch—lies over the root of the left lung. At this stage (5th week) the pleural passage or cavity is still in communication with both pericardial and peritoneal cavities. Its communication with the pericardium closes at the end of the 6th week.

respiratory expansion and contraction of the body-wall; naturally the most yielding part of the lung is acted on. In birds the anterior or respiratory part of the lung has been sharply demarcated from the posterior or "bellows" part. The latter is broken up into abdominal air sacs. In mammals the "bellows part," represented by the pulmonary infundibula and air sacs, is disseminated amongst the "respiratory" tissue, and the bronchi are arranged in such a way as to permit every part of the lung to undergo expansion. Thus the pattern of the bronchial tree is determined by the nature of the respiratory movements. Whereas only the respiratory part of a bird's lung is supradiaphragmatic, the whole of the mammalian lung occupies this position.

The Manner in which Lungs grow.—We have just said that the expansile units have become disseminated throughout the mammalian lung. It is manifest, however, that every part of the lung is not equally capable of expansion; the structures in the root, the great bronchial, arterial and venous stems are comparatively inelastic. On the other hand, the peripheral parts of a lung, made up of air sacs and of their divisions (infundibula), with their surrounding capillary vessels and tissues, yield readily to every expanding and contracting respiratory movement. It is clear, then, that as the foetal lung grows to birth dimensions and, in post-partum life, as it attains adult dimensions, there must be some means of maintaining the expansile elements in the more superficial strata of the lung. Bronchi and main vessels are in a continual process of elongation. The manner in which the growth of the lung proceeds is illustrated in Figs. 432, *A* and *B*, taken from a research by Dr. J. L. Bremer [3]. In Fig. 432, *B*, is shown a section across a terminal bud in the subpleural tissue of the lung of a rabbit 3 days old. The bud consists of an infundibular passage ending in two alveoli. In each alveolus, although the capillaries on their walls are exposed, a part of each is still lined by respiratory epithelium (*R.E.*) that will presently bud to produce an extension of the system of lobuli.

In Fig. 432, *A*, a terminal lobule of the lung of a kitten 4 days old has been reconstructed. A terminal bronchiole (*Br.3*) ends in a growing expansion divided into sac, infundibuli and alveoli. The bronchiole has just received its muscular and adventitious coat from the larger bronchus of which it is a continuation. The coats (cross-hatched) are spreading into the wall of the terminal air sac that will presently become reduced to a bronchiole, or if a division takes place in the sac, then two bronchioles will be formed. Behind the ongrowing margin of the developing coats will be seen the remnants of former saccular outgrowths which have become submerged beneath the growing tunics. In this way the peripheral parts of a lung are being constantly enlarged and

circulation in the lung is increased ; capillary plexuses appear on the walls of the alveoli (Palmer). At this stage the child becomes viable.

Changes in the Shape of the Lung.—Even in the 6th week the lungs are merely glandular masses round the terminal parts of the bronchial outgrowths. As in the frog, the hilum at this time forms the apex of the lung. During the 2nd and 3rd months the lungs assume their definite shape (Figs. 430, 431). The upper lobe grows towards the neck, and an apical region is thus formed. The apex as it grows forwards may come against the great azygos vein, which thus sinks into its substance [5]. The diaphragmatic or basal surface is at first absent, but as the pleural cavities expand and the basis of the diaphragm is stripped from the

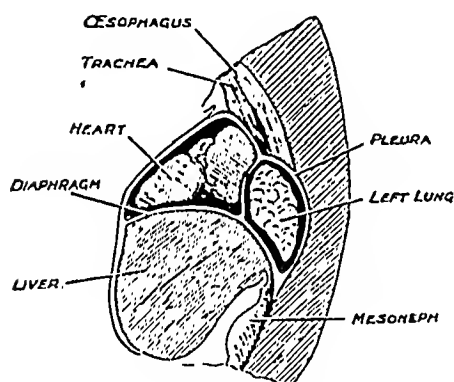


FIG. 430.

FIG. 430. The Position and Shape of the Lung in the 7th week of development. (After Prof. Frazer.)

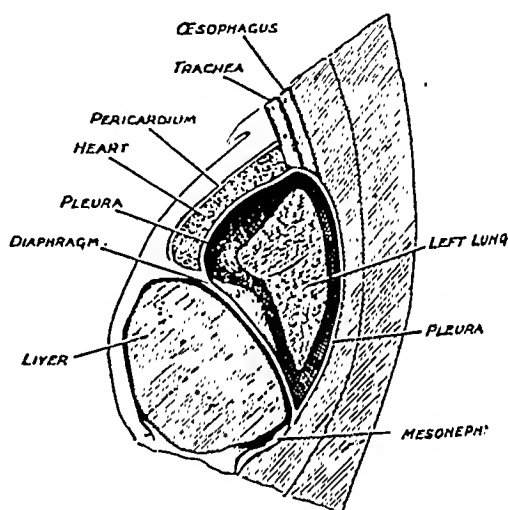


FIG. 431.

FIG. 431. The Position and Relationships of the Lung in the 9th week. (After Prof. Frazer.)

body-wall, this surface appears. In the human and anthropoid foetus the diaphragmatic or basal surface becomes remarkably large. The most important change, however, relates to the anterior or ventral border of the lungs ; at first situated on the dorsal side of the pericardium, the lungs expand forwards until they reach almost to the lateral borders of the sternum. In man and anthropoids the ventral or sterno-costal part of the lung reaches a high degree of development.

Evolution of Air Sacs.—In reptiles we see the original bladder-like lung becoming demarcated into two parts—an anterior or cephalic part with thick spongy walls that contain cellular recesses for air and are richly supplied with blood ; and a posterior, thin-walled and simple part. The thin-walled hinder part serves as a pulmonary bellows during the

of the development of the lungs of the pig. It must be remembered that the point of origin of any bronchus may easily be moved to meet new

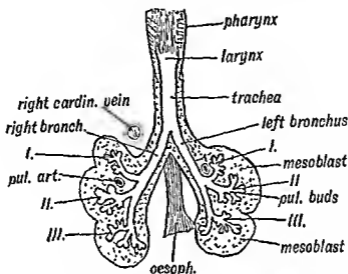


FIG. 433.—The Condition of the Right and Left Pulmonary Buds in an Embryo at the end of the 6th week (After His.)

physiological conditions. In the human embryo each main bronchus gives off three primary buds. All three remain separate on the right

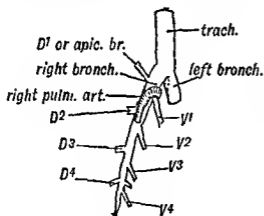


FIG. 434.

FIG. 434. Scheme of the Bronchial Ramifications in Quadrupedal Mammals. *D*, the dorsal ramifications; *V*, the ventral ramifications.

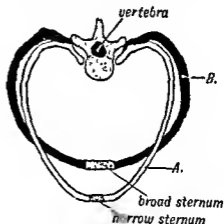


FIG. 435.

FIG. 435. Diagrammatic section of the Thorax of a Quadrupedal Mammal (*A*), contrasted with a corresponding section in Man (*B*).

side; on the left the upper and middle primary buds arise together (Fig. 431). Hence the upper lobe of the left lung represents the upper and middle lobes of the right. In the sheep and pig the upper right lobe springs from the trachea. The bronchus of the upper right lobe (the reason for it is not clear) commonly lies above its artery—that is

reformed, until the end of a child's 7th year, when all new formation ceases. Henceforth the process is one of expansion and consolidation of mature tissues. Even in the trachea buds may grow out and sometimes persist [6].

There are certain *peculiarities in the lungs* of animals which are adapted to an upright posture (Man and Anthropoids) :

(i) **Ramification of the Bronchi.**—In quadrupedal mammals the main bronchus passes backwards in the lung as a main stem, which grows gradually smaller by giving off four dorsal and four ventral bronchial

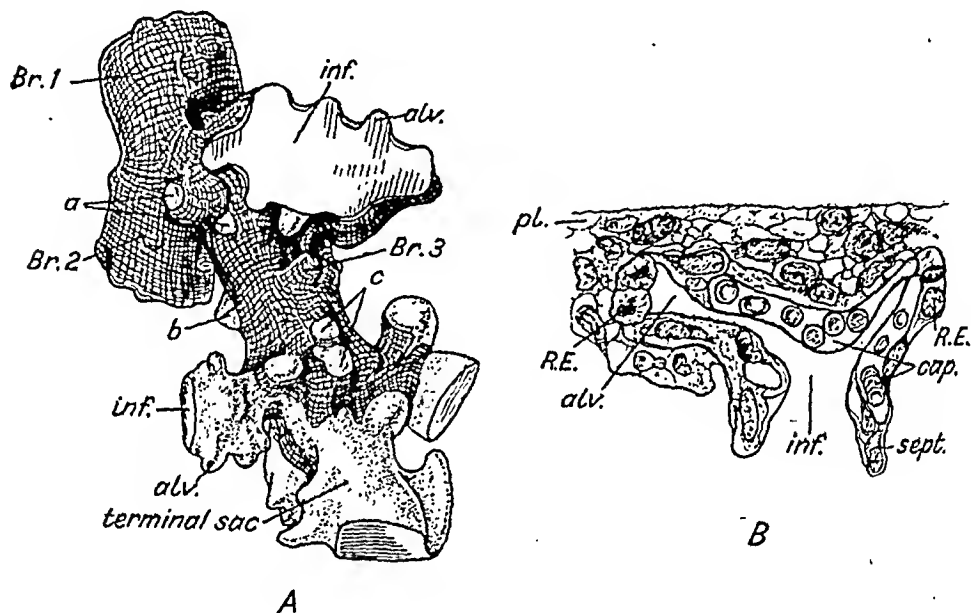


FIG. 432.

A. Terminal Bronchioles with Air Sacs from the Lung of a Kitten 4 days old (J. L. Bremer): Br. 1, Br. 2, Br. 3, the last being a terminal bronchiole ending in a sub-pleural sac, from which infundibula and alveoli are being developed. a, b, c, former infundibula and alveoli, which are being obliterated by the extension downwards of the muscular and connective coats along the bronchioles. The parts surrounded by these coats are cross-hatched.

B. Section across Terminal Alveoli (alv.) and an Infundibulum (inf.) in the subpleural tissue of a Rabbit 3 days old. pl., pleura; cap., capillary exposed in the wall of an alveolus; Sept., partition between infundibular passages; R.E., respiratory epithelium lining alveolus. (J. L. Bremer.)

branches (Fig. 434). So altered are the human lungs that the arrangement of bronchi seen in most mammals is not easily recognized in them. The ventral bronchi are larger, longer and more branched than in other mammals. In the human as in the mammalian lung the secondary and terminal bronchi are developed by division and subdivision of the pulmonary buds.

(ii) **Lobes of the Lungs.**—In the embryonic condition (Fig. 433) it is seen that the right and left lung buds are nearly symmetrical. Aeby supposed the upper lobe of the right lung to be absent in the left; and this is also the conclusion that Flint arrived at after a minute investigation

This lobe is always well developed in quadrupedal mammals. In them the pericardium is separated from the diaphragm by a diverticulum of the right pleura—the *sinus subpericardiacus* (Fig. 437). With the assumption of the upright posture (in man and anthropoids) the mechanism of respiration became altered and the heart came to rest on the diaphragm, the subpericardiac sinus and azygos lobe being thus obliterated. The reappearance of the azygos lobe as a separate structure—for a hurried rudiment is always present—in man is an *atavism*, that is to say, a recurrence of an *ancestral feature*. In quadrupeds an inspiratory contraction of the diaphragm is followed by an expansion of the lobus azygos and a corresponding elongation of the highly elastic intra-thoracic part of the inferior vena cava; in man, on the other hand, the con-

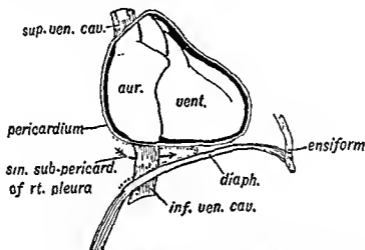


FIG. 437. The Relationship of the Heart to the Diaphragm in Quadrupedal Mammals.

traction of the diaphragm is followed by a descent of the conically shaped heart, thus indirectly enlarging the pulmonary space.

Blood Supply of the Lung.—The pulmonary aorta, with the ascending part of the aortic arch, is formed out of the truncus arteriosus (see p. 453). The right and left pulmonary arteries spring as branches from the right and left 6th aortic arches (Fig. 436). The lung buds are at first supplied by arteries arising from the dorsal aorta (Huntington), but in the 5th week this primary pulmonary plexus is joined by a communication from the 6th aortic arches, the anastomosis being the basis of the pulmonary arteries. At first the pulmonary arteries descend by the side of the trachea, but as the heart becomes intra-thoracic in the 6th and 7th weeks they are gradually shortened until they pass horizontally to the roots of the lungs [9]. The pulmonary veins grow out from the pulmonary buds and enter the left auricle through the venous mesocardium about the 5th week (Fig. 429). The mesenchymatous or interstitial tissue of

to say, it is *eparterial*. The other bronchi are *hyparterial* [7]. A clue to the asymmetry of the right and left lungs will be found in a fuller knowledge of the mechanism of respiration [8].

(iii) **Diameters of the Thorax.**—The peculiar branching of the bronchi in man and orthograde primates is due to the shape of the lungs, which in turn is due to the shape of the thorax, and this in its turn is determined by the mode of breathing. In quadrupedal animals, such as the horse or dog, in which the chest rests and is supported between the fore limbs, the thorax has its greatest diameter in the dorso-ventral direction (Fig. 435). In orthograde animals (man, anthropoids, and also in some water-

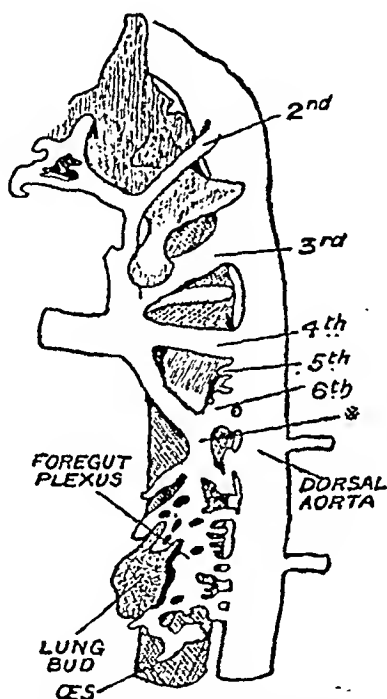


FIG. 436. Showing the Origin of the Blood Supply to the Lung, in Cat Embryo. (Huntington.) * = pulmonary artery.

living mammals, such as seals, etc.) the transverse diameter becomes the greater. At birth the diameters of the child's thorax are nearly equal. The thorax is flattened by the spine becoming invaginated within it; the thorax thus comes to lie within the axis of gravity of the upright body.

(iv) **Azygos Lobe.**—On the inner side of the right lung of man the azygos lobe is frequently present, sometimes as a mere pulmonary projection or trace, sometimes as a lobule. It represents an over-development of the 2nd ventral branch from the right bronchus (Fig. 426). It projects into and fills a slight recess between the pericardium and diaphragm, behind the intrathoracic part of the inferior vena cava.

(iii) the false-vocal cords and ventricles; these structures came into being with the evolution of the mammalian stem.

In Fig. 438 the basis of the epiglottis is being assembled at the anterior fornix of the primitive laryngeal orifice; it is derived from the posterior part of the hypobranchial eminence (Fig. 422, *C.M.*) and like the thyroid cartilage is made up chiefly from the substance of the 4th arch. The primitive lateral folds, which guard the orifice, are becoming covered over by convex folds which are rising upwards; the arytenoid cartilages are being developed in the hinder parts of these folds, the apices of the cartilages pointing towards the epiglottis. In Fig. 439 is represented a stage reached in the 7th week; the epiglottis is becoming separated from the tongue; the aryteno-epiglottidean folds have assumed a bent

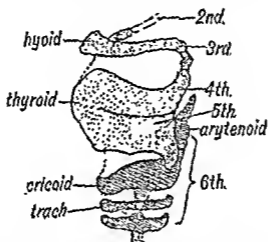


FIG. 440. Diagram of the Cartilages of the Larynx to show the parts derived from the skeleton of each visceral segment.

form, so that the new orifice to the larynx has, when closed, the shape of the letter T. The aperture to the larynx is now opened by the arytenoid cartilages—by being drawn backwards from the epiglottis and at the same time pulled apart.

Thyroid Cartilage.—The origin of the cartilages of the larynx is shown in Fig. 440. The thyroid cartilage is formed by the expansion and amalgamation of the skeletal bases of the 4th and 5th visceral arches; at least this is true of lower mammals, but in higher mammals only the 4th is involved (Edgeworth). The skeletal basis of the 6th or pulmonary arch in man, which forms the two lateral cartilages in the short pulmonary passage of the frog, becomes divided into a dorsal segment that forms the arytenoid cartilage, a ventral segment to form the cricoid. From the posterior part of the primitive lateral cartilage arise the rings in the wall of the trachea, chief, secondary and ultimate bronchi (Fig. 440).

Prof. Frazer has made a very thorough investigation of the develop-

the lungs is supplied by the bronchial arteries, which represent the primary vessels of the lung buds (Fig. 436). These arteries also supply the pleura on the mediastinal and diaphragmatic surfaces of the lungs. Lymphatic vessels begin to invade the root or hilum of the lungs at the end of the 2nd month, spreading into the lobes along the vascular beds. They reach the subpleural tissues in the 3rd and 4th months [10].

Changes at Birth.—When a child begins to breathe at birth, the expansion of the lungs helps to open up the pulmonary circulation; the foramen ovale is shut and the ductus arteriosus is closed, and within the 1st month becomes reduced to a fibrous cord (see p. 463). The ductus arteriosus represents the dorsal segment of the 6th left arch; the corresponding part of the 6th right arch disappears soon after it is formed. Before birth the air spaces are filled by amniotic fluid; it is

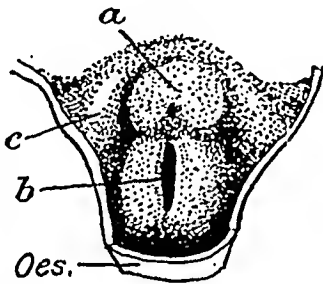


FIG. 438.

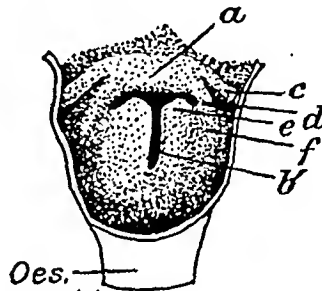


FIG. 439.

FIG. 438. The Epiglottis and Folds flanking the Upper Aperture of the Larynx as seen in the 6th week. (After Prof. Frazer.)

FIG. 439. The Epiglottis and Aryteno-epiglottidean Folds in the 7th week. (After Prof. Frazer.)

a, epiglottis; *b*, primary laryngeal opening; *b'*, secondary laryngeal opening; *c*, remnant of 4th pharyngeal arch; *d*, aryteno-epiglottidean fold; *e*, apex of arytenoid; *f*, derivative from pulmonary arch.

not until about the 4th day after birth that the whole of the lung is inflated and the fluid absorbed. The first part to expand is the costosternal or ventral part; the second, the diaphragmatic or basal part, the apex is the third, and the dorsal border and deeper parts the last.

Evolution of the Larynx [11].—In lung-breathing fishes the larynx consists of two lateral movable folds which guard the pulmonary orifice in the floor of the pharynx; they also regulate the intake and output of air. It is in this form that the larynx appears in the human embryo (Fig. 422); the folds which guard the respiratory chink become the true vocal cords; the chink itself becomes the opening between the vocal cords—the glottis. During the 6th and 7th weeks there is built up over the embryonic glottis a superstructure to protect the vocal cords and the opening into the respiratory passage [12]. This superstructure (see Figs. 438, 439) consists of (i) epiglottis; (ii) aryteno-epiglottidean folds;

form the ventricles. In the 5th month mucous glands are developed from the membrane lining the ventricles, and a little later an outgrowth is developed from their apices to form the sacculles of the larynx. They project against the thyro-hyoid membrane. Occasionally the *sacculle* of the larynx may protrude through the thyro-hyoid membrane, thus giving rise to an air cyst in the neck [15]. Laryngeal air-sacs are normally developed in anthropoids after birth, and attain a great size in the adults, extending to the chest and axillae. Their function is unknown.

Mechanism of Respiration [16].—The *diaphragm* constitutes one of the most pronounced structural characteristics of mammals. The ancestral mammalian types in which the diaphragm first appeared are long since extinct; we cannot study the evolution of the diaphragm among modern vertebrates. There are certain facts that throw light upon its origin and make us certain that the diaphragm did not grow within the coelom as a partition to shut off the part which contains the lungs from the part containing the abdominal viscera. During the 4th and 5th weeks of development the pleural cavities are represented merely by the two short passages leading from the pericardial to the peritoneal cavity. In the 5th week these passages lie in the cervical region under the 4th and 5th spinal segments, from which the phrenic nerve arises, and from which the musculature of the diaphragm is derived. It is clear, then, that the diaphragm entered into the service of the lungs when these were situated, as in the frog, below the cervical region (Fig. 423). In some manner, as the lungs developed and afterwards took up a thoracic position, the muscle that became associated with them in the neck accompanied them when they retreated to their new position in the thorax. If we are to find a representative of the early form of the diaphragm, it must be amongst amphibians that we should look. We can also get light on its origin by studying certain malformations to which it is liable in man [17].

In Fig. 441 is shown the thoracic aspect of the diaphragm of a newly born child, in which the left *pleuro-peritoneal opening* has remained patent. Through the opening the upper end of the left supra-renal body and the spleen project within the pleural cavity, giving rise to a congenital diaphragmatic hernia. The pleuro-peritoneal openings are situated on each side, between the muscular fibres which rise from the ribs and sternum, and which form the *ventro-lateral* part of the diaphragm, and the muscular fibres which arise from the spine and arcuate ligaments, forming the *dorsal* part of the diaphragm. The phrenic nerves, when they reach the diaphragm, divide into two branches, a ventral to the right and left ventro-lateral parts (from IIIrd and IVth cervical nerves), and a dorsal branch (from IVth and Vth cervical nerves) to the right and left dorsal parts [16]. The central tendon, situated between the four

ment of the larynx [12]. At each side of the primary pulmonary orifice lies a mass of tissue representing the last or 6th visceral arch (Fig. 422). In this tissue develop the various parts of the larynx. The cricoid and arytenoid are the primary cartilages; they are the only ones present in the larynx of amphibia and reptiles. The thyroid appears in mammals only. As already pointed out, the true vocal cords represent the primary opening of the larynx. In the 2nd and 3rd months of human development the part of the laryngeal cavity above the vocal cords (suprarimal part) is produced by the upgrowth of the lateral masses on each side of the primary opening. In these masses are developed the arytenoid cartilages and the aryteno-epiglottidean or permanent folds which bound the lateral margins of the secondary laryngeal orifice.

The muscles within the larynx are derived from the sphincter of the primitive oesophagus. When the pulmonary outgrowth takes place a ventral part of the primitive sphincter (in reality a constrictor of the pharynx) is separated to serve as a sphincter for the new orifice. The nucleus of its nerve is part of the nucleus ambiguus and its nerve fibres issue in the accessory part of the XIth. The sphincteric fibres give rise to the thyro-arytenoid and inter-arytenoid muscles and also to the crico-thyroid, the latter receiving its nerve supply from the inferior laryngeal. The dilator mechanism, represented by the posterior crico-arytenoid muscles, is later in its evolution and development than the constrictor mechanism.

In lower vertebrates the lateral margins of the epiglottis extend into the aryteno-epiglottic folds. The cartilages of Santorini and Wrisberg, in the aryteno-epiglottic folds, are continuous with the epiglottis in many mammals (Sutton). Until the 5th month of foetal life the epiglottis lies behind the palate and within the naso-pharynx—a position which is normal for the adults of all orders of mammals [13].

The purposes which the larynx serves in all air-breathing vertebrates are: (i) to regulate the inflow and outflow of respiratory air, and thus the positive and negative pressure within the lungs; (ii) to prevent food and drink from passing into the air passage. The production of voice, which has led to a marked alteration of the human arytenoid cartilage, represents a secondary function of the larynx. The acquisition of articulate speech has been attended by a domination of the cerebral cortex over the muscles of the larynx. Only in man and the higher anthropoids are the true vocal cords covered by stratified epithelium; but all the muscles of the human larynx are represented in the larynx of the ape, although in a less specialized condition [14].

Soon after the lateral masses grow up to form the suprarimal cavity of the larynx, an evagination takes place above each vocal cord to

Were the parts of this sheet restored to their embryonic relationships, then the pericardium should be placed beneath the mandible, so that the central tendon of the diaphragm lies opposite the 4th cervical segment. If we are to restore parts to their original positions, the sternal and costal origins of the ventro-lateral segment of the diaphragm should be detached in the thorax and the muscle placed ventrally in the neck so that it is continuous, at its insertion to the septum transversum, with the depressors of the hyoid bone. Behind, the detached thoracic origins of the sternal and costal fibres should become continuous with the anterior end of the rectus sheet. In the human body the anterior part of the

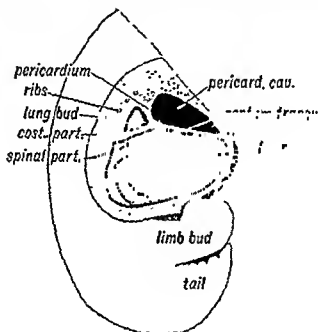


FIG. 1

rectus sheet becomes divided into four strata—(i) the ventro-lateral fibres of the diaphragm, (ii) the interchondral parts of the intercostals, (iii) the rectus abdominis, which in all mammals except man and the anthropoids reaches forwards to the 1st rib, (iv) the pectoralis major, minor, subclavius and that frequent human abnormality the *sternalis* muscle. The development of the lung separates the deepest part of the rectus sheet from the chest wall to form the ventro-lateral part of the diaphragm (see Figs. 430, 431). As we have seen (p. 109) the rectus sheet is derived from the ventral unsegmented mesoderm. Its segmentation is secondary. The ribs are formed in the chest wall and to the posterior six this part of the diaphragm ultimately obtains an attachment.

parts just mentioned, makes up the fifth morphological element of the diaphragm. Each of these five parts—the central, the two dorsal and two ventro-lateral, has its own developmental history.

The *central tendon of the diaphragm* is formed from the septum transversum (Fig. 442). The manner in which that structure is cleft into its pericardial and diaphragmatic elements by the outgrowth of the two pleural passages and lung buds is indicated in Figs. 442, 443 and 444. The dorsal and ventral mesenteries of the fore-gut (Fig. 444) are included in the formation of the septum transversum (p. 384), and hence the

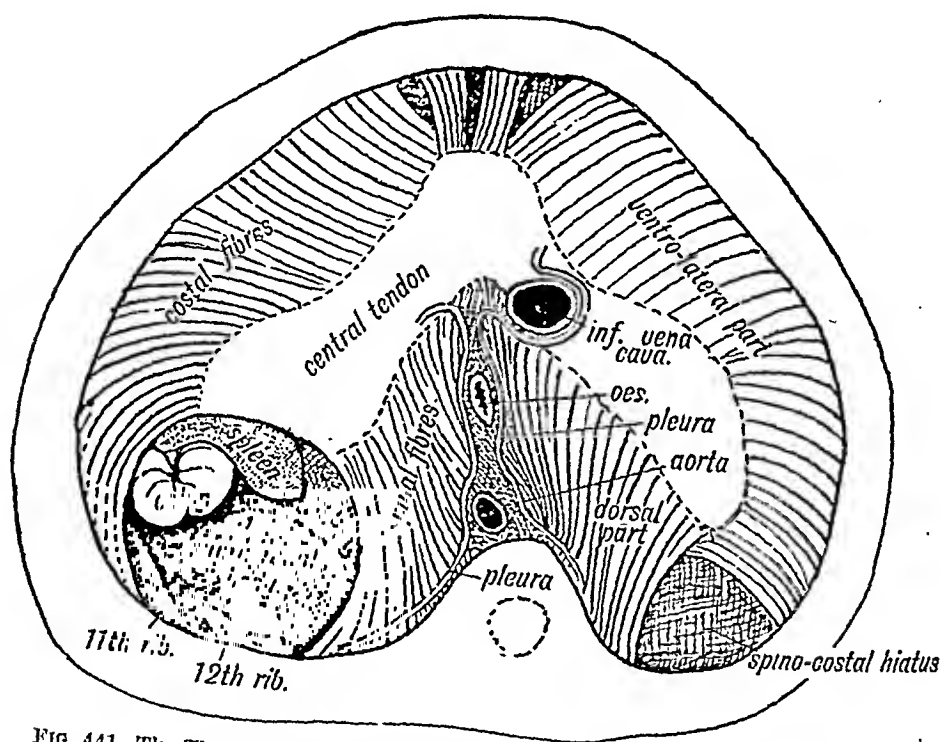


FIG. 441. The Thoracic Aspect of the Diaphragm of a Newly-born Child in which the communication between the Peritoneum and Pleura has not been closed on the left side; the position of the opening is marked on the right side by the Spino-costal Hiatus. The dorsal mesentery of the fore-gut (represented by the posterior mediastinal pleura) is also shown.

structures developed in these mesenteries—the aorta, oesophagus, zygous veins, thoracic duct, vagus nerves and inferior vena cava—perforate the median or central part of the diaphragm. The structures of the posterior mediastinum lie in the mesentery of the fore-gut (see Figs. 441, 444).

The *ventro-lateral parts* of the diaphragm arise as right and left *pleuro-peritoneal folds*, being developed from the inner stratum of the body-wall—the fold of the right side being seen in Fig. 443. Each fold is derived from the ventral longitudinal muscular sheet which also gives rise to the rectus abdominis and depressors of the hyoid bone (Fig. 423).

Were the parts of this sheet restored to their embryonic relationships, then the pericardium should be placed beneath the mandible, so that the central tendon of the diaphragm lies opposite the 4th cervical segment. If we are to restore parts to their original positions, the sternal and costal origins of the ventro-lateral segment of the diaphragm should be detached in the thorax and the muscle placed ventrally in the neck so that it is continuous, at its insertion to the septum transversum, with the depressors of the hyoid bone. Behind, the detached thoracic origins of the sternal and costal fibres should become continuous with the anterior end of the rectus sheet. In the human body the anterior part of the

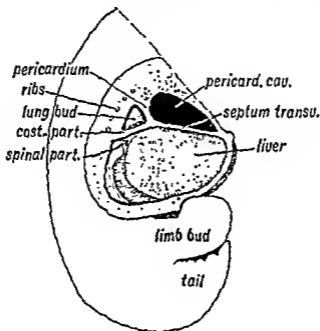


Fig. 430. A. Ventral portion of the embryo.

rectus sheet becomes divided into four strata—(i) the ventro-lateral fibres of the diaphragm, (ii) the interchondral parts of the intercostals, (iii) the rectus abdominis, which in all mammals except man and the anthropoids reaches forwards to the 1st rib, (iv) the pectoralis major, minor, subclavius and that frequent human abnormality the *sternalis* muscle. The development of the lung separates the deepest part of the rectus sheet from the chest wall to form the ventro-lateral part of the diaphragm (see Figs. 430, 431). As we have seen (p. 109) the rectus sheet is derived from the ventral unsegmented mesoderm. Its segmentation is secondary. The ribs are formed in the chest wall and to the posterior six this part of the diaphragm ultimately obtains an attachment.

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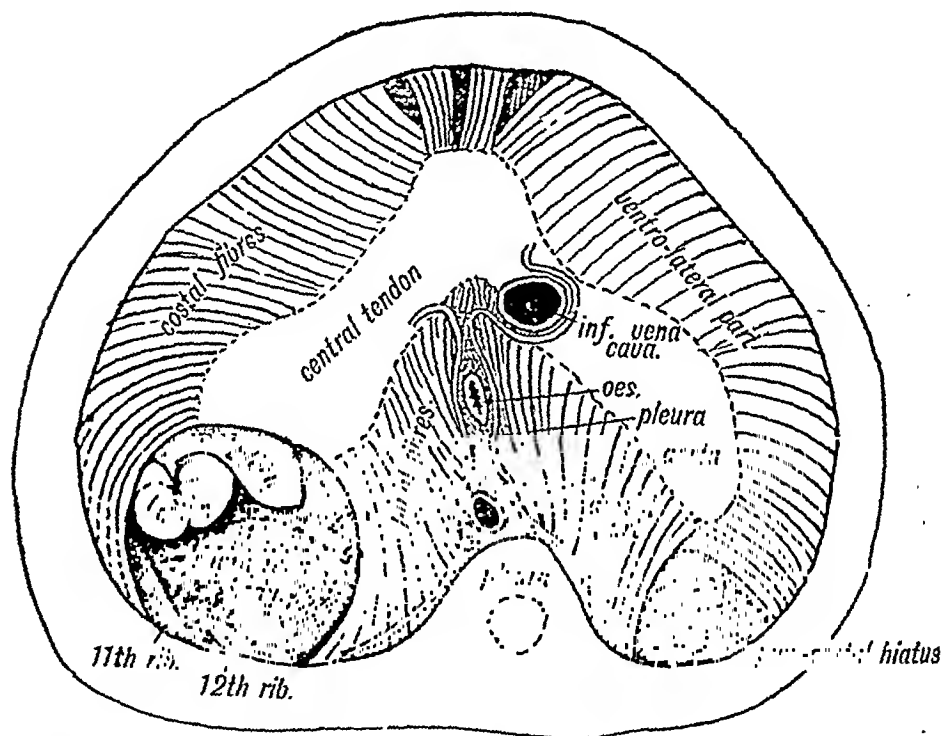


FIG. 441. The Thoracic Aspect of the Diaphragm of a Newly-born Child in which the communication between the Peritoneum and Pleura has not been closed on the left side; the position of the opening is marked on the right side by the Spino-costal Hiatus. The dorsal mesentery of the fore-gut (represented by the posterior mediastinal pleura) is also shown.

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(i) The spinal fibres, at their origin from the vertebrae, migrate outwards and obtain attachment to the arcuate ligaments; the costal fibres

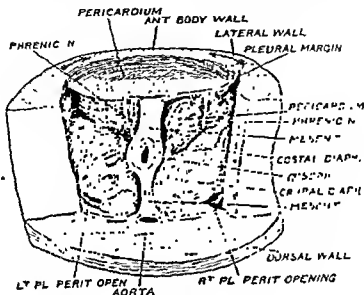


FIG. 444 A dorsal view of the hinder parts of the Developing Pleural Cavities in the Thoracic Wall

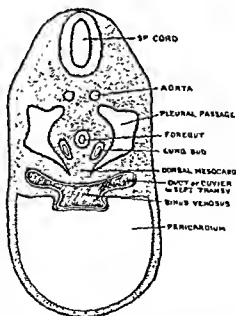


FIG. 445. Section across Mesentery of the Fore-gut to show its relationship to the Pleuro-peritoneal Openings and Septum Transversum

migrate inwards, obtaining an origin from the 11th and 12th ribs. Only in man and anthropoids does this migration occur, and the extent

The *dorsal parts of the diaphragm* are derived from that portion of the transversalis sheet of the body-wall that forms the subvertebral musculature (Figs. 423, 441). The manner in which these parts of the diaphragm are detached from the body-wall and carried into the thorax by the developing pleural cavities and lungs is shown in Figs. 442, 444. The right and left spinal parts of the diaphragm sink within the dorsal mesentery of the fore-gut, obtaining anteriorly an insertion to the pericardium and septum transversum, while posteriorly they retain an origin from the spine and costal processes. The quadratus lumborum, longus

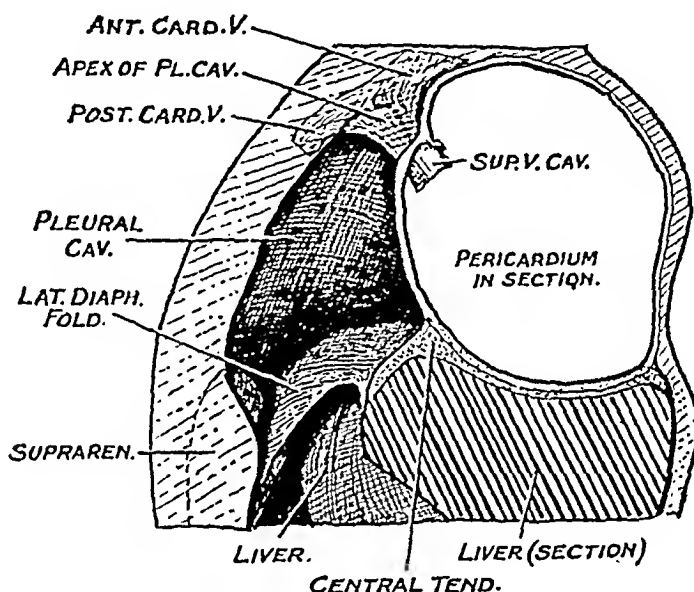


FIG. 443. The Right Pleuro-peritoneal or Diaphragmatic Fold being separated from the Body-Wall and in the 7th week of development. (After Prof. Frazer.) *Pleural cav.*, right pleural cavity; *apex of pl. cav.*, apex of pleural cavity extending dorsal to the right duct of Cuvier (superior vena cava).

colli, the rectus capitis anticus major and minor are also derived from the subvertebral musculature.

Pleuro-peritoneal Openings [18].—The pleural passages, into which the lung buds develop at the end of the 1st month, open into the pericardium by the itinera venosa; behind they communicate with the peritoneum by the pleuro-peritoneal openings (Figs. 427, 441, 444). These lie above the septum transversum (Fig. 445) and are separated by the mesentery of the fore-gut. In the mesentery between the openings are developed the spinal fibres of the diaphragm; on the lateral side of each opening arise the costal fibres. The condition of the pleuro-peritoneal openings in the 7th week, when they are on the point of closing, is shown in Figs. 342, 444. The actual closure is effected by that form of embryological healing to which the name of zygoxis has been given (p. 407), but certain accessory factors are also involved in approximating their margins.

[7] Prof. Frazer (*Manual of Embryology*) regards the eparterial position of early stage of development the artery position. See also Prof. Appleton's the apical region of the lungs (*Jour.*

[8] For literature on the morphology of bronchi, see: Huntington, G. S., *Amer. Jour. Anat.*, 1920, 27, 99; Keith, Sir A., in Hill's *Further Advances in Physiology*, 1909.

[9] For literature on the morphology of bronchi, see: Gaudin, P. D., *Contrib. Emb.*, 1932, 1, 1; Zeitsch. Anat. Entwickl., 1932, 98, 760; Conn and Others, *Anat. Rec.*, 1942, 83, 335.

[10] Harvey and Zimmerman, *Anat. Rec.*, 1935, 61, 203.

[11] For the evolution of the larynx, see: Negus, V., *Acta Oto-Laryng.*, 1932, 17,

[12] Frazer, J. E., *loc. cit.*

[13] Negus, V., *Jour. Anat.*, 1928, 62, 1. Mr. Negus regards the epiglottis as concerned in smelling rather than with the act of swallowing.

[14] Duckworth, W. L. H., *Jour. Anat.*, 1913, 47, 82.

[15] Many cases are on record. For a recent report, see Campbell, J. M., *Jour. Anat.*, 1938, 72, 465.

[16] For the evolution of the diaphragm, see: Keith, Sir A., references given in notes [3], [8]; Marcus, H., *Anat. Anz.*, 1937, 84, 161 (genesis of diaphragm).

[17] For structure and abnormalities of diaphragm, see: Blair, D. M., *Jour. Anat.*, 1923, 57, 203; Keith, Sir A., *ibid.*, 1905, 39, 243; *Brit. Med. Jour.*, 1910, 1, 1297; Contat, C., *Ann. d'Anat. Path.*, 1933, 10, 1; Garraud and Bartiez, *ibid.*, 1936, 13, 603; Hayek, H. von, *Zeitsch. Anat. Entwickl.*, 1933, 100, 218; Hill, W. C. O., *Brit. Jour. Surg.*, 1939, 26, 632. For development of diaphragm:

[18] For development of the pleural cavities, see McGaw, W. H., *Anat. Rec.*, 1924, 28, 105; Heuser, C., *Contrib. Emb.*, 1930, 22, 140.

to which they approach each other and thus close the opening is extremely variable. (ii) The collapsed condition of the lungs of the foetus allows the abdominal viscera, developed in the domes of the diaphragm, to press the spinal and costal fibres against the dorsal wall of the thorax, thus mechanically closing the aperture. The liver, especially by its upgrowth within the septum transversum, helps to close the apertures, particularly on the right side, which is seldom the site of a diaphragmatic hernia. The supra-renal bodies are also developed just behind the pleuro-peritoneal orifices (Fig. 442), and help to close them. Indeed, the mesentery of the Wolffian body, in the anterior extremity of which the supra-renal bodies develop, is attached along the dorsal wall of the coelom as far as the septum transversum, where it forms a fold upon the lateral or outer margin of the pleuro-peritoneal orifice.

Musculature of the Body-Wall.—The development of the musculature of the body-wall, also of the ribs and sternum, ought rightly to be included here, for all are closely related to the mechanism of respiration. The ribs have been already considered, and it will be more convenient to reserve the development of the wall of the thorax and abdomen with other correlated structures for another chapter (Chapter XXVIII).

NOTES AND REFERENCES

[1] I am assuming that swim bladders appeared first and that lungs were derived from them, but the opposite opinion has been sustained (see Ballantine, Miss F. M., *Trans. Roy. Soc. Edin.*, 1927, 55, 371).

[2] See references given in note [2], Chapter VII.

[3] For recent accounts of the development of the lungs, see: Miller, W. S., *The Lung*, 1947 (a record of 47 years of investigation); Frazer, J. E., *Manual of Human Embryology*, 1940; Broman, I., *Anat. Anz.*, 1938, 86, 225; Bremer, J. L., *Contrib. Emb.*, 1935, 147, 83; Willson, H. G., *Amer. Jour. Anat.*, 1928, 41, 97; Puiggros-Sala, J., *Zeitsch. Anat. Entwickl.*, 1937, 106, 209 (early stages in development of human lung); Strukow, A. I., *ibid.*, 1932, 98, 466 (late stages in development); Clements, L. P., *Anat. Rec.*, 1938, 70, 575 (in pig); Palmer, D. W., *Amer. Jour. Anat.*, 1936, 58, 59 (late foetal stages); Keith, Sir A., *Jour. Anat.*, 1905, 39, 243 (a theory of pulmonary evolution).

[4] Authorities agree that alveoli, in early stages of development, have a complete epithelial lining, but many are of opinion that later such lining is partial or absent, capillaries in their walls being uncovered. On this point, see: Macklin, C. C., *Jour. Anat.*, 1935, 59, 188; *Archiv. Path.*, 1936, 21, 202; Josselyn, L. E., *Anat. Rec.*, 1935, 62, 147; Bensley, R. and S., *ibid.*, 1935, 64, 41; Loosli, C. G., *Amer. Jour. Anat.*, 1938, 62, 375; Jeker, L., *Anat. Anz.*, 1934, 77, 65; Ropes, M. W., *Contrib. Emb.*, 1930, 22, 79; Allen, C. M., *Zeitsch. Anat. Entwickl.*, 1932, 98, 466.

[5] The part of the apex of the right lung cut off by the fissure containing the great azygos vein has been erroneously named the "azygos lobe." For recent records of this anomaly, see Cairney, J., *Jour. Anat.*, 1924, 58, 54; Stibbe, E. P., *ibid.*, 1929, 63, 303. For an account of the true azygos lobe, see p. 488.

[6] Bremer, J. L., *Anat. Rec.*, 1932, 54, 361.

wall of the tubule itself. The secretion of the tubules is conveyed to a common collecting duct—the *nephric duct*—which ends in the cloaca.

An inspection of Fig. 446 (*B, C, D*) will show how the various parts of the nephric tubule just named arise from the wall of the intermediate part of the coelom. We have already seen (p. 59) how, in the 4th week, the mesoderm on each side of the embryo becomes demarcated transversely into body segments or somites, and also longitudinally into the paraxial mass, the intermediate cell mass and the parietal laminae, and how extensions of the coelom are included in each of these longitudinal divisions. From Fig. 446 it will be seen that a nephric tubule arises by

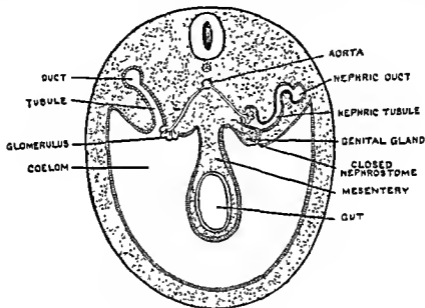


FIG. 447. Schematic section to show the specialization of the Dorsal Part of the Coelom.

an evagination of the outer wall of the intermediate part of the coelom, while the glomerular chamber or nephrocele (*c*) and the peritoneal funnel are produced from the coelomic passage which originally connected the peritoneal cavity with the cavity of a somite. Thus the nephridial and genital systems must be regarded as modified parts of the wall of the original coelomic cavity [1].

Succession of Renal Systems.—In the evolution of the higher vertebrates there has been a succession of three renal systems, the third being the present functional system—the *kidneys* or *metanephros*. All of them, *pronephros*, *mesonephros* or *Wolffian body* and *metanephros*, are compounded of the same system of nephridial elements, just as the milk and permanent teeth are successive manifestations of the same dental system.

CHAPTER XXV

UROGENITAL SYSTEM

Evolutionary Stages.—The association of the genital with the urinary system has to be sought for in the ancestry from which vertebrate animals arose, for even in the lowest vertebrates they are already associated. The evidence of embryology makes it certain that man has been evolved from a type in which each segment of the body was provided with its own excretory tubule or kidney. The parts of an excretory or *nephric tubule* are diagrammatically represented in Fig. 446, *A*. Into its dilated head or beginning projects a vascular body—a *glomerulus*—

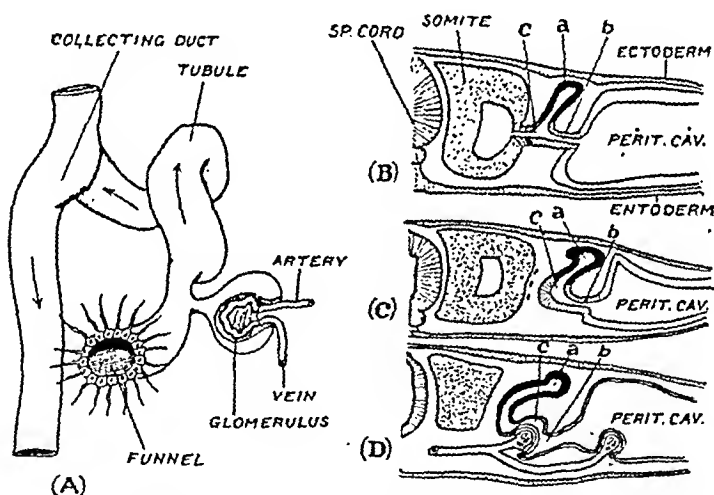


FIG. 446. Composition and Origin of Nephric Tubules.

- A. Diagram of an isolated nephric tubule. (After Semon.)
- B. Showing the manner in which the intermediate cell mass (*a, b, c*) gives origin to the nephric tubule (*a*), peritoneal funnel (*b*) and the nephrocele (*c*).
- C. The isolation of these parts from the somite and their union to form a system.
- D. The origin of a glomerulus in the wall of the nephrocele (*c*). (After Felix.)

similar to the glomeruli of the kidney; at its commencement the tubule is also connected with the peritoneal cavity by an open funnel-shaped structure—the *peritoneal funnel*. By this communication ova or spermatozoa, which are shed from the genital glands, may escape from the peritoneal cavity and enter the excretory tubules, and thus pass outside the body. We shall see that the openings by which ova still escape in women and the passages by which semen leaves the testicle in men are derived from the funnel elements of the nephric tubules. The essential part of the excretory organ is the epithelial-lined

Wolffian Body or Mesonephros (Fig. 448).—In lower vertebrates (Fishes and Amphibians) the Wolffian body is the functional kidney; in higher vertebrates (Reptiles, Birds and Mammals) it is merely a temporary or embryonic structure, the renal function being taken over by the permanent kidney. Apparently the permanent kidney (metanephros) arose by a hypertrophy and separation of the hindermost segment of the Wolffian body. The presence of the mesonephros in the human embryo and in the embryonic stages of the three great classes of higher vertebrates, with the presence of many curious stages in the development of

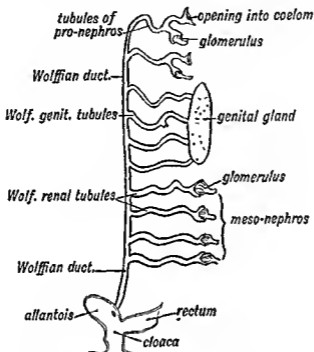


FIG. 449. Scheme of the Wolffian Body of the right side.

their genito-urinary system, can be explained only by the fact that these higher forms are descended from ancestors of the lower.

In Fig. 449 is given a diagrammatic representation of the tubular composition of the Wolffian body of the frog, which in many points correspond to those of the human embryo. Each body is made up of a main duct and a series of tubules. In the frog, as in the human embryo, the hind-gut ends in a dilatation, the *cloaca*. In the cloaca open the rectum, allantois or bladder, and the two *Wolffian ducts*—right and left. In the frog, the Wolffian bodies lie on each side of the spine, their anterior ends reaching forwards to the region of the heart. Each duct is joined by numerous convoluted tubules—the *Wolffian* or *nephric tubules*. Each tubule is furnished with a glomerulus at its blind extremity, and in most features agrees with a secretory tubule—such as is seen in the

In the human embryo of the 6th week all three systems may be seen; while the pronephric system, which is developed in the last four or five cervical segments and first two or three thoracic, is then undergoing retrogression, the metanephric in the anterior sacral segments is only appearing; in this week the mesonephric system is approaching the height of its development, extending from the 7th cervical to the 3rd lumbar segment.

It is clear that pronephros, mesonephros and metanephros are parts of the same linear series of organs. Not only so, but as we shall see presently, the duct of the pronephros, as it grows backwards, has a power of "induction" on the tissues of the mesonephros, bringing about an organization of that body. All three bodies are made up of nephric

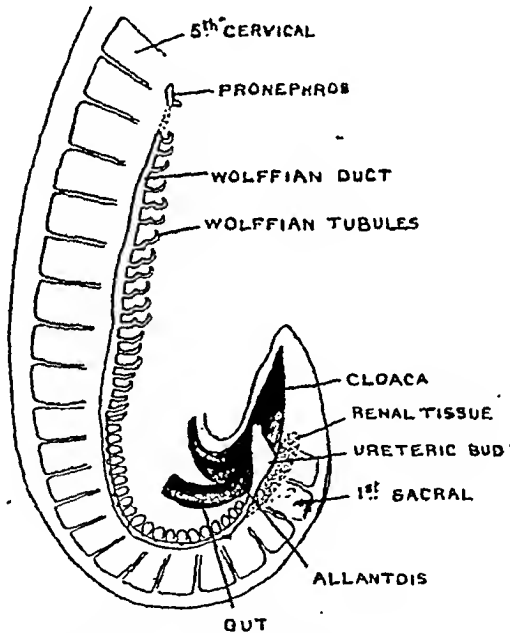


FIG. 448. Condition of the Nephric or Renal System in a Human Embryo of 4 weeks. (After Ingalls.)

tubules opening into a common excretory (Wolffian) duct. While in the cervical region the tubules are simple and retain their segmental arrangement, in the dorsal and lumbar region they multiply in number and complexity; in the sacral region they become exceedingly numerous and massed round a diverticulum from the Wolffian duct—which forms the primitive ureter. In the 2nd month of human development the Wolffian body is at the height of its development and in the latter part of this month and in the early part of the 3rd is actually functional (excretory). In the 3rd month the permanent kidney assumes its predominant position, and its predecessor, the Wolffian body, is converted into a mere appendage of the genital system.

Wolffian Body or Mesonephros (Fig. 448).—In lower vertebrates (Fishes and Amphibians) the Wolffian body is the functional kidney; in higher vertebrates (Reptiles, Birds and Mammals) it is merely a temporary or embryonic structure, the renal function being taken over by the permanent kidney. Apparently the permanent kidney (metanephros) arose by a hypertrophy and separation of the hindermost segment of the Wolffian body. The presence of the mesonephros in the human embryo and in the embryonic stages of the three great classes of higher vertebrates, with the presence of many curious stages in the development of

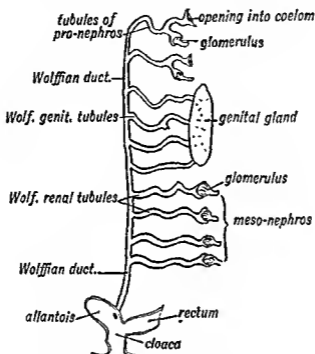


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permanent kidney. These tubules are concerned in the separation of urine; the Wolffian duct conveys the urine from the tubules to the cloaca. The anterior tubules, however, lose their secretory function and become associated with the genital gland. In the male frog they convey the spermatozoa to the Wolffian duct, which thus carries both urine and spermatozoa. The most anterior of all, as will be seen in Fig. 449, remain unattached. This is also the case in the human embryo. In the female, the *genital* Wolffian tubules are connected with the ovary, but are quite functionless.

Wolffian Body in the Human Embryo [2].—By the middle of the 2nd

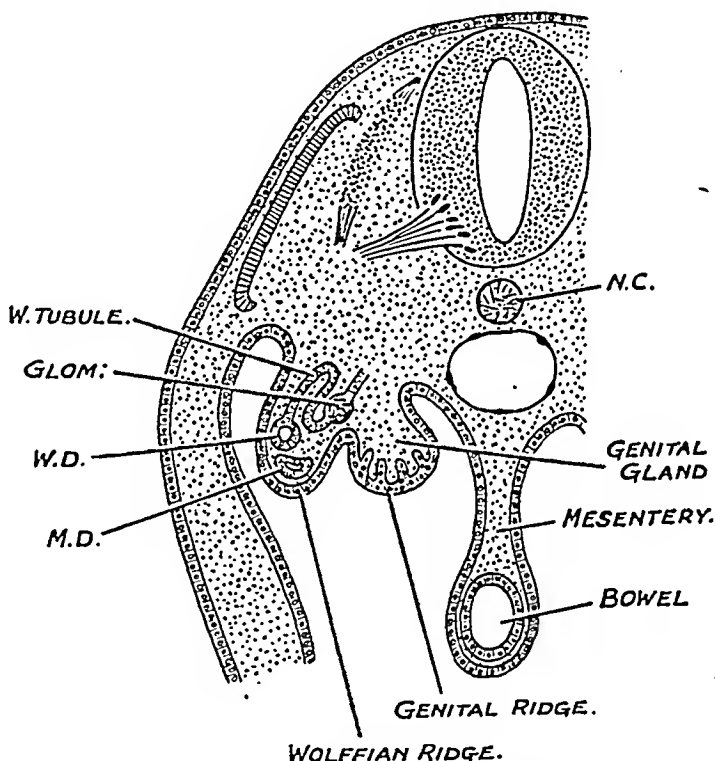


FIG. 450. Diagrammatic section to show the Position of the Wolffian and Genital Ridges on the Dorsal Wall of the Abdomen. W.D., Wolffian duct; M.D., Müllerian duct; Glom., glomerulus; W. tubule, Wolffian tubule; N.C., notochord.

month of foetal life, the Wolffian body is well developed; by the end of that month it is undergoing a process of atrophy, except those parts which come to be connected with the genital glands. Originally extending from the 5th cervical to the 4th lumbar segment, by the 8th week the Wolffian bodies are confined to the region of the lower three thoracic and upper three lumbar vertebrae, where they project into the abdominal cavity on each side of the dorsal attachment of the mesentery (Fig. 450). Its anterior end lies at the pleuro-peritoneal orifice of the diaphragm. To its inner side, in the lower dorsal region, lies the *genital ridge*. The

genital and the Wolffian hodies have each their own mesentery, but these two mesenteries have a common attachment—the common urogenital mesentery (Fig. 450). On section the Wolffian ridge is seen to be made up of convoluted tubules terminating at their blind extremities in glomeruli. The tubules open into the Wolffian duct, just as in the frog; the duct is situated on the lateral margin of the ridge, dorsal to the Müllerian duct. It runs backwards in this ridge and turns into the pelvis to end with the Müllerian duct (also situated in the Wolffian ridge) in the cloaca of the hind-gut (Fig. 448). The whole arrangement is similar to that seen in the frog. Further, as in the frog, certain of the more anterior or genital tubules are connected with the genital glands, and are not, as the posterior are, secretory in nature. If the testes were functional at this time—which they are not—the spermatozoa and urine of the Wolffian body would pass to the cloaca by the Wolffian duct.

Origin of the Wolffian Duct and Tubules.—The tubules which compose the Wolffian body are developed in the *intermediate cell mass*, in the manner already described (p. 501). The intermediate cell mass, in the anterior part of the body, is divided from before backwards into segments; two or three tubules arise in each segment, but in the posterior part of the body the intermediate cell mass remains unsegmented, forming a continuous column known as the *nephrogenic cord*. The tubules, although of the nature depicted in Fig. 446, appear in the course of human development as minute vesicles in the intermediate cell mass; these vesicles become tubular; one end opens into the Wolffian duct; at the other a glomerulus is developed (Fig. 451). The duct is developed in the outer (lateral) part of the intermediate cell mass. Its anterior or cervical part appears early in the 4th week as a solid rod of cells formed by the union of the terminal ends of the pronephric tubules. By the end of the 4th week the caudal end of the pronephric duct has reached the cloaca and thus the pronephric duct forms the basis of the Wolffian duct—the duct into which the tubules of the Wolffian body open. Indeed, the Wolffian duct is not only a direct continuation of the pronephric duct, but it has to be remembered that the latter when it enters the region of the mesonephros exercises an inductive influence on that body, stimulating the formation of Wolffian tubules [3]. At first the hinder or pelvic ends of the Wolffian bodies are some distance apart, but in the 8th week these pelvic parts become approximated and come to lie together in a common sheath known as the *genital cord*. The genital cord contains the terminal segments of the Wolffian and Müllerian ducts. The Müllerian ducts, which become median in position, fuse to form the uterus (Fig. 461).

The Pronephros [3].—The pronephric tubules differ from the mesone-

phric in retaining open peritoneal funnels (Fig. 449) and in their having glomeruli occasionally situated within the peritoneal cavity (Fig. 447). They reach their highest development in anterior segments of the human embryo during the 4th week, and then disappear, leaving no trace. Their duct becomes the Wolffian duct, and if a remnant did persist we should seek for it at the commencement of this duct. The

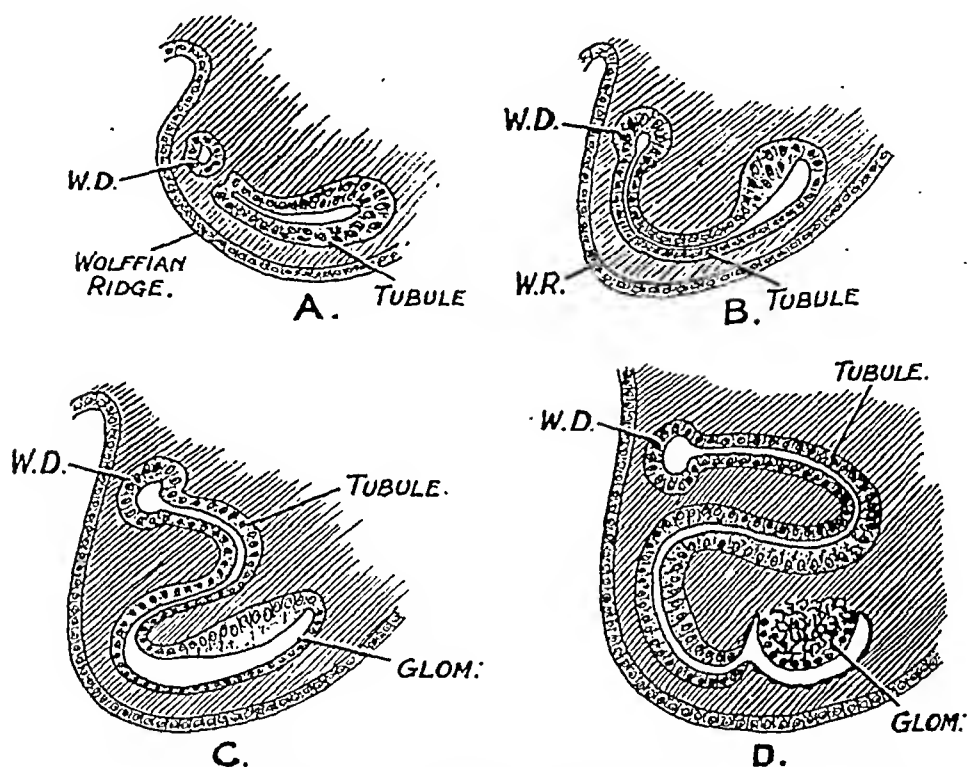


FIG. 451. Four Stages in the Development of a Wolffian (Nephric) Tubule in the Human Embryo. (Shikunami.)

- A. Vesicular stage of tubule.
- B. Tubule joins Wolffian duct (W.D.).
- C. Becomes convoluted.
- D. A glomerulus is developed.

Tubule, Wolffian tubule; *W.D.*, Wolffian duct; *Glom.*, glomerulus; *W.R.*, Wolffian ridge.

pronephros is the renal organ in amphioxus and the lamprey. It is functional in the tadpole.

Fate of the Wolffian Body.—The various remnants of the embryonic renal formation that may persist in the adult female are shown in Fig. 452. The Müllerian duct, the upper part of which becomes the Fallopian tube, is situated in the Wolffian ridge (Fig. 450). Hence when the ovary and tube take up their position in the pelvis, the Wolffian mesentery, which comes to form the mesosalpinx, is also drawn within the pelvis and with it all the Wolffian remnants. A hydatid attached to the mesosalpinx (part of the broad ligament) at the fimbriated extremity

of the Fallopian tube (Fig. 452) represents the most anterior (cephalic) part of the Wolffian formation and may be pronephric in origin (see Fig. 449). The Wolffian duct (Fig. 452) runs towards the body of the uterus in the mesosalpinx; it reaches the side of the uterus, but from that point onwards it has disappeared by the commencement of the 3rd month [4]. Occasionally, however, remnants of the lower or distal part of the duct persist. They lie in the roof of the vagina. The point of termination of the duct is sometimes preserved in the vulva to the side of the opening of the vagina and just outside the hymen. Only the upper part of the duct (mesosalpingeal part) usually persists in women. The uterine and vaginal segments, when they persist, get the

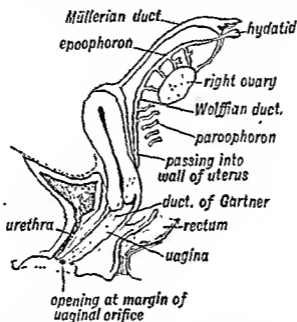


FIG. 452. Remnants of the Wolffian Body in the Female (see also Fig. 454).

name of *duct of Gartner*. The *genital* tubules, those attached to or connected with the ovary, persist and form the *epoöphoron*, Organ of Rosenmüller, or parovarium. The *renal* Wolffian tubules—those which acted as renal structures in the embryo—also persist, sometimes unconnected with the duct. They lie between the ovary and uterus and form the *paröphoron*. Fluid may collect in their cavities, and thus those vestiges may form cysts, but, as we shall see (p. 410), the Wolffian remnants which are the usual source of cystic formations in the female lie along the ovarian fimbria and are derived from the elements which give rise to the rete testis in the male [5]. We shall see that the female hormone (oestrin) arrests or causes atrophy of the parts of the Wolffian ducts which are genital in function.

In the *male* [6] the Wolffian duct forms (Fig. 453): (i) the tube of the epididymis, which is coiled up in the globus major, body and globus minor of the epididymis; (ii) the vas deferens and common ejaculatory duct; the duct opens at each side of the uterus masculinus in the prostatic urethra, a site corresponding to the vestibule of the vagina in the female; (iii) the vesiculæ seminales arise from the Wolffian ducts as tubular diverticula at the end of the 3rd month; the terminal part of the duct also becomes dilated to form an ampulla; (iv) we shall see that the ureter and collecting tubules of the kidney also arise from the Wolffian duct. The stalked hydatid frequently seen on the upper

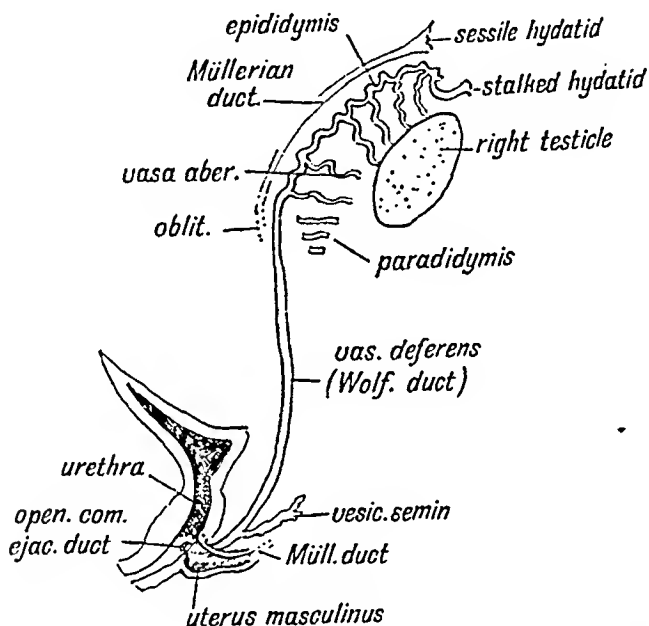


FIG. 453. Remnant of the Wolffian Body in the Male (see also Fig. 452).

extremity of the testicle corresponds to the hydatid at the fimbriated extremity of the Fallopian tube in the female, and is of similar origin (Figs. 452 and 453).

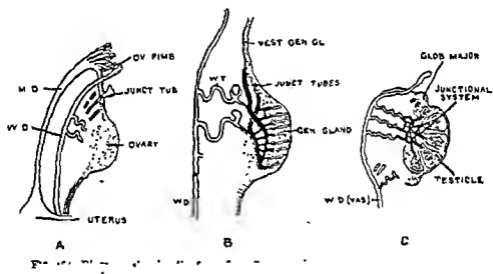
The *genital tubules* of the Wolffian body become the vasa efferentia and coni vasculosi. Out of the total series of Wolffian tubules, about eighty in number, only ten retain their connection with the duct and effect a union with the testis.

The *renal tubules* of the Wolffian body form: (i) the vasa aberrantia found in the globus minor; (ii) the paradidymis or organ of Giraldés situated in the cord above the globus major, but not always present. The vas aberrans represents an elongated Wolffian tubule, which has effected a communication with the Wolffian duct, but not with the genital gland. The tubules of the paradidymis represent blind tubules, which

retain the embryonic cystic form. All these tubules, both genital and renal of the Wolffian body, are situated originally in the mesentery of the Wolffian body (Fig. 450). The male hormone stimulates the development of the Wolffian duct, while it arrests Müllerian development.

Thus it will be seen that while in the male the Wolffian tubules and duct become part of the genital system, in the female they become functionless and only of pathological importance. Their presence in woman is due to their utility in her male progeny, just as breasts persist in the male because of their utility in female progeny.

Rete Testis.—The junction between the genital tubules of the Wolffian body and the seminal tubules of the testes is effected by the development of a separate element to which the names of rete-cords or junctional



cords have been given. In Fig. 454, B, is represented the origin of the junctional tubules, according to the account given by Dr. Allen [7]. The ovary and testis represent only the middle part of the original genital ridge; the anterior and posterior parts atrophy and disappear by the end of the 2nd month. In the anterior vestigial part of the ridge solid cords representing peritoneal funnels (Fig. 446) grow into the mesentery of the Wolffian body, and from these cords, as shown in Fig. 454, B (where only two cords are represented), is formed the rete testis. The rete testis effects communications with the seminal tubules by means of outgrowths, which form the vasa recta, and also with the glomerular or blind extremities of the genital tubules of the Wolffian body (Fig. 454, C). In the female the junctional cords are formed in and near the hilus of the ovary; vestiges usually remain. Frequently

fimbriated hydatids (peritoneal funnels) are attached to them (Fig. 454, *A*). The majority of parovarian cysts [8] are formed from the junctional rudiments. Isolated vestiges may also be seen in the testicle between its upper pole and the globus major (Fig. 454, *C*). They also may give rise to cysts.

THE KIDNEY

Origin of the Permanent Kidney [9].—In Fishes and Amphibians the Wolffian body alone acts as a kidney. In Reptiles, Birds and Mammals the permanent or hind kidney appears and supplants the Wolffian kidney. Like the Wolffian body, the kidney arises by the combination of two elements which are developed separately—a duct or collecting

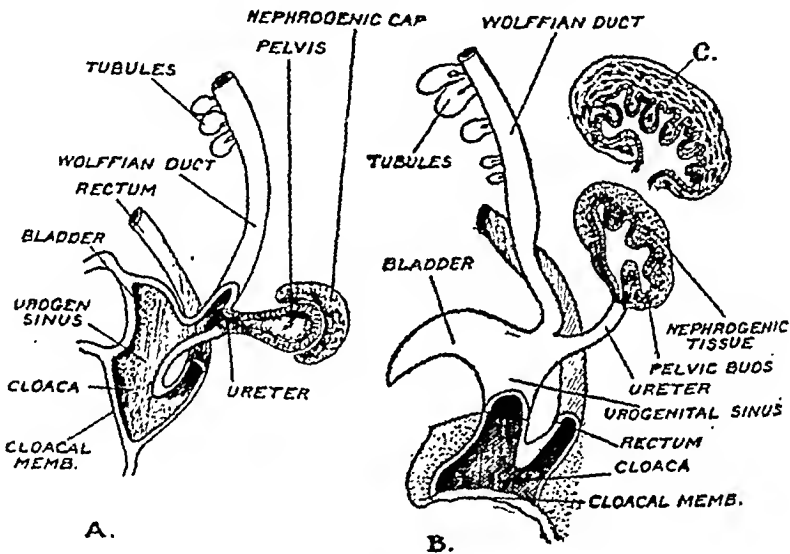


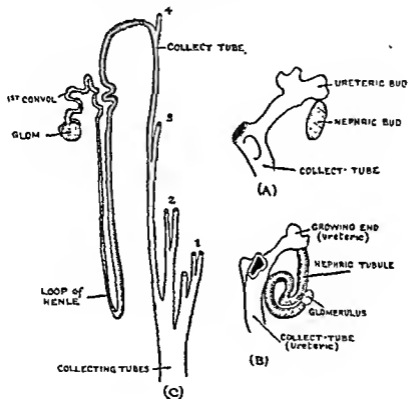
FIG. 455.

A. The Ureteric Bud and Nephrogenic Cap early in the 6th week.

B. The same parts later in the 6th week. *C* indicates the stage of renal development reached in the 7th week.

system and a nephric or secretory system. The collecting system arises as an outgrowth from the hinder end of the Wolffian duct, and forms the ureter, the pelvis of the kidney and the collecting tubules, which compose the main part of the medullary pyramids of the kidney. The secretory part arises from the hinder end of the nephridial system, the *nephrogenic cord*—just behind the part which gives origin to the mesonephros and on a level with the 1st and 2nd sacral segments; it forms the cortex of the kidneys: the glomeruli, convoluted tubules and loops of Henle; in short, the secretory substance of the kidney (Fig. 456). Already, at the beginning of the 5th week, the ureteric part of the kidney is apparent as a dilatation or slight evagination at the hinder end of the Wolffian duct, near the cloaca (Fig. 448). The stage reached by the beginning of the 6th week is shown in Fig. 455, *A*; the ureteric bud is stalked, the stalk

representing the ureter and its dilated pelvic end the renal pelvis and collecting tubules. The nephrogenic tissue forms a cap on the pelvic dilatation. At this time the kidney lies under the 4th and 5th lumbar segments. At a later stage in the 6th week (Fig. 455, B) the ureteric stalk has become elongated, the pelvic dilatation has given rise to primary evaginations representing the calyces of the kidneys; round the evaginations is massed the nephrogenic cap. The kidney now lies dorsal to the Wolffian body and under the 2nd and 3rd lumbar segments.



FIG

The separation of the ureter from the Wolffian duct has commenced. In Fig. 455, C, a still later stage is shown. Tubules now begin to form in the nephrogenic cap and collecting tubules to arise from the pelvic bud. Collecting tubules increase in number by the division and redivision of the growing end of the pelvic outgrowths. In the 3rd month the increase of collecting tubules continues; the growing end of each bud divides and redivides, and in this manner the collecting tubules of the pyramids are formed (Fig. 456, C). In Fig. 456, A, the growing extremity of such a collecting duct is represented; in Fig. 457 a series of such buds is shown on the surface of a growing kidney. Near

one of its terminal buds is represented one of the numerous tubule-rudiments, formed from the nephrogenic tissue surrounding the ureteric outgrowths (Fig. 456, *A*). Like a Wolffian tubule, it appears in a vesicular form. At one extremity it establishes a communication with the collecting tubule; at the other a glomerulus develops (Fig. 451). The tubule elongates, becomes convoluted and quickly assumes the adult form represented in Fig. 456, C. Glomeruli begin to appear at the commencement of the 3rd month; each is formed out of a nucleus of

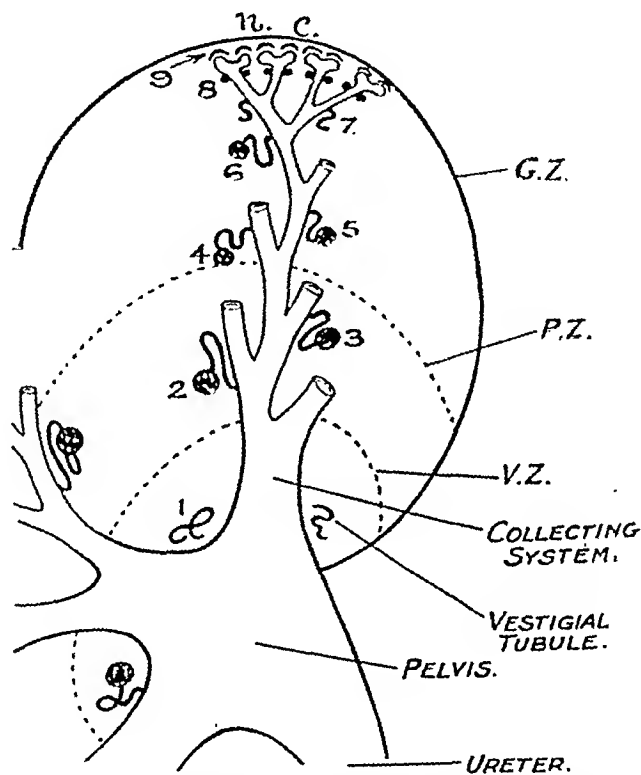


FIG. 457. Section of Part of a Foetal Kidney showing the Subcapsular Zone of Growth (G.Z.). The numbers 1-9 represent the different divisions. P.Z., zone of proliferation; V.Z., zone of vestigial tubules; they serve for a time; G.Z., growth or nephrogenic zone.

nephrogenic tissue in which an afferent artery ends in a cluster of capillaries. Like the teeth, glomeruli are developed full sized. Late in the 3rd month loops of Henle are developed, separating the upper from the lower convoluted segments of a nephric tube. With the development of the loops of Henle, a kidney becomes functional. The term "nephron" comprises the glomerulus, the first convoluted segment, the loop of Henle and the second convoluted segment. A capsule becomes differentiated for the kidney from the surrounding mesodermal tissue in the 3rd month. The kidneys have by then reached their final position—extending from the 11th thoracic to the 4th lumbar segment. Up to

the time of birth, tubular and glomerular formation are seen in full activity within the subcapsular zone of the kidney (Fig. 457). The deep tubules are the first to differentiate. The earlier broods of collecting tubes degenerate [10]; by the time of birth the buds on the cortical surface of the renal pyramids represent the 15th or even the 20th in the divisional series. Soon after birth the formation of new elements ceases; increase in size is then due to pure growth of the parts already formed [11]. The collecting tubules, arising from each primary evagination of the ureteric bud, become massed in pyramids; the bases of the pyramids, clothed by nephrogenic caps, appear on the surface of the kidney and give it a lobulated structure. In the fissures between the lobules cortex is formed; soon after birth, as new cortical tissue is laid down, the depressions between the lobules are filled up. In many mammals (ox, bear, seal) the renal substance remains broken up into numerous lobules. Man is peculiar among primates in having his renal substance divided into a number of pyramids; in the great apes—as amongst monkeys—there is usually only one great papilla, whereas in man there are 8-12 papillae; each papilla may have two or more secondary pyramids attached to it [12].

The upper pole of the kidney reaches the 11th rib in the 5th month, and is in juxtaposition with the adrenal, which is developed at the anterior end of the Wolffian body. At their first appearance the renal buds receive temporary branches from the common iliac artery and from the aorta, but when they come to lie on the dorsal aspect of the Wolffian body in the 7th week, the arterial network supplying the tubules of that body invades the nephrogenic tissue of the renal buds and thus the kidneys annex the series of Wolffian arteries—stretching from the 11th thoracic to the 4th lumbar. The definite arteries are derived from those of the 2nd lumbar segment, but frequently more than one pair persist [13].

Changes which affect the kidney during the 3rd month, both as regards its position and in its relationship to neighbouring structures, are illustrated in Figs. 458, A, B. In the 9th week (A), the posterior wall of the abdomen is occupied, from above downward, by adrenal, kidney and ovary, the kidney being overshadowed in size by its two neighbours. By the end of the 12th week changes have taken place and are shown in Fig. 458, B. The kidneys and adrenal bodies remain in their places in the loins, but the ovary and uterus, having retained their pelvic position, are far removed from them. The kidneys are larger both relatively and absolutely. The ureter has undergone elongation. These changes are due to the growth and elongation of the lumbar and sacral segments of the vertebral column. The earlier stages in the development of the

ureter, its separation from the Wolffian duct and its implantation in the bladder will be described later (p. 533).

As the kidney grows forwards in the 2nd month its hilum at first looks towards the pubic region, and even when it has reached its final position and the poles become upper and lower, the hilum of the kidney still looks towards the ventral wall of the abdomen. In the 4th and 5th month an anterior lip is formed to the hilum by the development of cortical tissue, and the hilum then assumes its normal form and position [14]. The anterior lip is usually absent from *horseshoe kidneys*, an abnormality which arises from a fusion of the right and left nephrogenic buds [15]. Such kidneys are usually supplied with multiple renal arteries. In other cases the renal buds grow not towards the loins but towards the sacral region, becoming developed in the pelvis, drawing

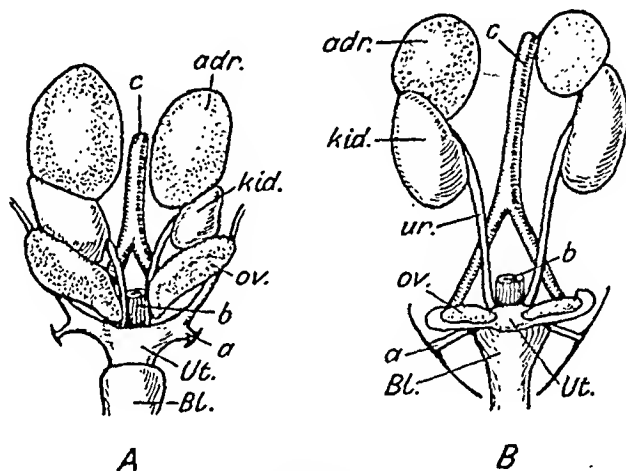


FIG. 458.

A. Structures occupying the Posterior Wall of the Abdomen of a Female Foetus in the 9th week of development, showing the position and size of the Kidneys. (Bankert.)

B. The same in the 12th week. (Bankert.)

a, round ligament of uterus; b, the rectum; c, abdominal aorta; adr., adrenal; kid., kidney; ov., ovary; Ut., uterus; ur., ureter; Bl., bladder.

their arteries from the sacral and iliac vessels. The ureteric bud may divide and give rise to a forked ureter, or to double or even triple ureters [16]. The nephrogenic element may remain single or it also may become divided, giving rise to two kidneys on one side. Another common developmental error is the failure of the nephric tubules to effect a union with the collecting tubules. The nephric tubules then become dilated and cystic, giving rise to *congenital cysts* of the kidney [17].

Kidneys may fail to develop. Dr. Boyden [15] injured the posterior growing end of the Wolffian duct and observed that the kidney on the same side failed to develop. Dr. O'Connor inflicted a similar injury to the pronephric duct [3] and so arrested the development of the meso-

nephros. Certain breeds of rats are liable to produce young in which one or both kidneys may fail to form, this condition being known as renal agenesis [18].

The Uterus.—We have finished our consideration of the parts derived from the Wolffian body and its duct and pass on to note how the uterus and its tubes arise in the human embryo and foetus. At first sight it may appear that in passing to the development of the uterus we have entered a new section. In one sense this is true, but in another it is not, for in their origin and development the Müllerian ducts which provide a basis for the uterine system are closely linked with those of the Wolffian ducts. The Wolffian ducts as they form seem to "induce" the development of their Müllerian companions.

The *Müllerian Ducts* or *Oviducts* are present in almost all vertebrates, and convey the ova from the peritoneal cavity to the surface of the body.

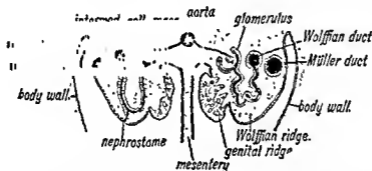


FIG. 450. Diagrammatic section across the Wolffian and Genital Ridges to show the Origin and Relations of the Müllerian Duct to the Duct and Tubules of the Wolffian Body. (After Pasteau)

In fishes, amphibians, reptiles, birds and lower mammals (Marsupials) the ducts terminate in the cloaca. This is also the case in the embryonic stages of man and all higher mammals. The development [19] of the duct in man is very simple. The first part to be formed is the ostium abdominale, which appears on the ventro-lateral aspect of the Wolffian ridge (Fig. 450).

The

the Wolffian ridge (under the 3rd thoracic segment), represents a modified peritoneal funnel or nephrostome. From the apex of the invagination of coelomic epithelium, a solid rod-like process of cells grows backwards on the Wolffian ridge, ventral to the Wolffian duct (Fig. 450), reaching the region of the cloaca in the 8th week. Although the ostium is developed thus, the fimbriae that surround it are not formed until the 3rd month, when they appear as outgrowths of the lining membrane of the tube. More than one ostium may be developed, representing neighbouring nephric funnels. As it grows backwards in the Wolffian

ridge to reach the pelvis the Müllerian duct passes ventral and medial to the Wolffian duct (Fig. 460) and comes in contact with its neighbour of the opposite side in the pelvis (Figs. 461, 462). The Müllerian duct is formed in the embryo later than the Wolffian duct; its posterior growing end does not reach the urogenital sinus until the 8th week. Within the pelvis there is a median fold of peritoneum and of subperitoneal tissue, surrounding the terminal parts of the Wolffian and Müllerian ducts, making up the structure known as the *genital cord*. The right and

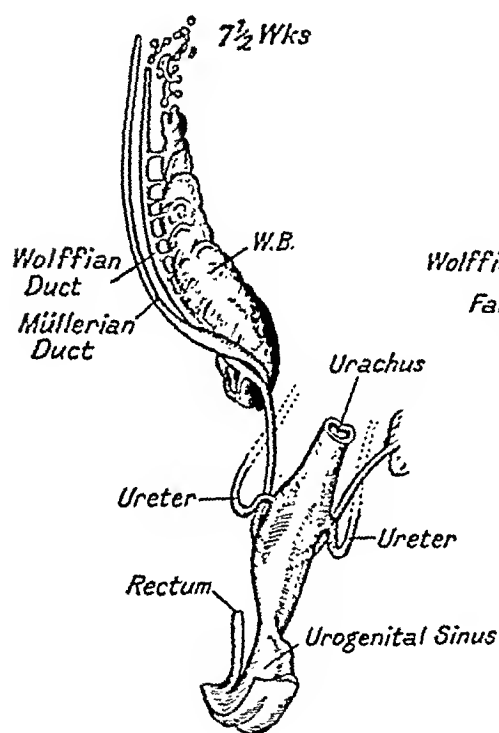


FIG. 460.

FIG. 460. The Genital System of a Female Human Foetus in the 7th week of development. (R. H. Hunter.) The growing lower end of the Müllerian duct is entering the "genital cord." W.B., Wolffian body; only that of the right side is depicted.

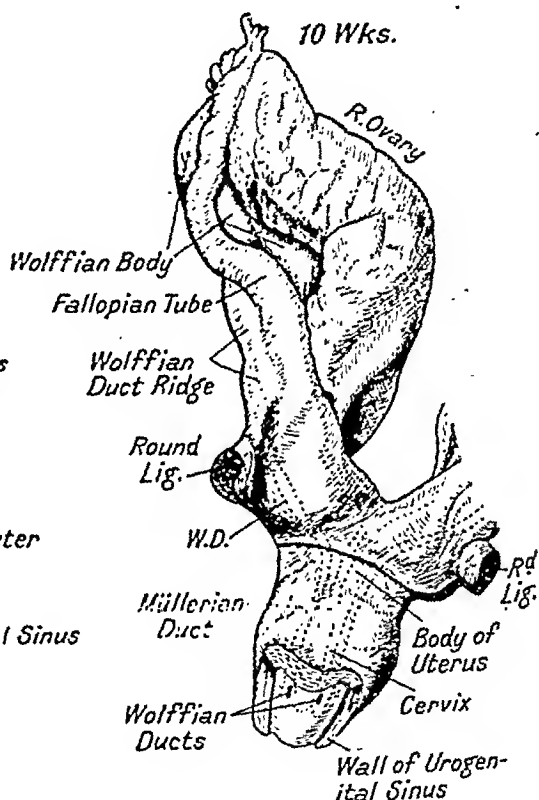


FIG. 461.

FIG. 461. The Genital System of a Female Human Foetus in the 10th week of development. The lower ends of the Müllerian and Wolffian ducts are shown by stippled lines. (R. H. Hunter.)

left Müllerian ducts enter the cord side by side and fuse together, but do not acquire a lumen until late in the 3rd month, when they open on the dorsal wall of the uro-genital sinus, a derivative of the cloaca (Figs. 460, 461). The opening of the two Müllerian ducts is situated between those of the Wolffian ducts (Figs. 461, 462). Round the terminal parts of the Müllerian ducts, where they merge with the posterior (dorsal) wall of the urogenital sinus, there is an area or clump of actively growing tissue, made up of mesoderm and also of epithelium derived from the

lining of the Müllerian ducts. This proliferating mass is known as the *Müllerian bulb*; we shall see that it is the active agent in the formation of the vagina. There are corresponding structures at the termination of the Wolffian ducts known as *Wolffian bulbs*; these are concerned with the downward prolongation of the Wolffian ducts and with the formation of parts to be noted later.

Müllerian ducts, although they reach their full development only in women, are yet as completely and strongly formed in the male embryo of the 7th week as in the female of a corresponding age. By the beginning of the 3rd month the fimbriated end of the tube has retreated to the level of the 2nd lumbar segment.

Genital Septum or Cord.—During the 3rd month the Müllerian ducts

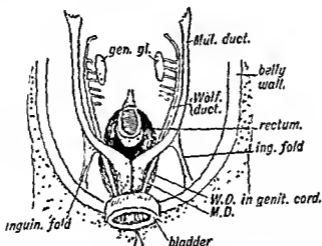


FIG 462. Diagram of the Müllerian Ducts at the commencement of the 3rd month. Ventral view.

show two distinct stages in their course: (i) *Lumbar*, which lies in the Wolffian ridge and is suspended from the posterior abdominal wall by the Wolffian mesentery. This stage afterwards forms the Fallopian tube (Figs. 461, 462). (ii) *Pelvic*, which is embedded in the genital septum or cord in which the uterus and vagina are fashioned. The posterior ends of the Wolffian ridges, with their contents, the Wolffian and Müllerian ducts, fuse in the pelvis during the 8th week, the genital septum or cord being thus formed. With their fusion the peritoneal space of the pelvis is separated into a deep posterior part—the pouch of Douglas and a shallow anterior depression—the utero-vesical. The parts of the Müllerian ducts within the cord form the uterus and vagina. The ureter is also enclosed within the mesodermal tissue of the genital cord, but afterwards becomes separated from it.

The genital cord of the foetus at the beginning of the 3rd month shows the two Müllerian and two Wolffian ducts—in the male as well as in the

female (Fig. 461). One of the first signs of sexual differentiation is to be observed in the genital cord. Whereas the genital cord in the male embryo is closely applied to the bladder, so that there is no utero-vesical pouch, in the female the cord remains separated from the bladder by a deep peritoneal pocket.

The *Round Ligament of the Uterus*, which becomes apparent early in the 3rd month, is attached to the Müllerian duct on each side (Figs. 461, 462). The point of attachment marks the junction of the uterine and Fallopian segments of the Müllerian ducts. The round ligament corresponds to the *gubernaculum testis* in the male and its development is similar. Both are developed in the manner described below.

Plasticity of the Sub-peritoneal Tissue.—Part of the Wolffian ridge is continued backwards as a peritoneal fold to the groin, this part forming the *inguinal fold* (Fig. 462). Within the inguinal fold and within the mesenteries of the Wolffian body and of the genital gland are contained inclusions of the subperitoneal tissue, which in the pelvic region of the abdomen is particularly rich in nonstriated muscle. We have seen the part which the subperitoneal tissue plays in the fixation of the organs and mesenteries in the upper region of the abdomen. It is endowed with plastic properties. This is more especially the case in the pelvic region of the abdomen—particularly within the genital septum or cord, which affords a nidus for the development of uterus and vagina and of uterine ligaments. The inguinal fold contains an extension of the subperitoneal sheet. The mesodermal tissue, in the lower end of the inguinal fold, is continued through the abdominal wall external to the deep epigastric artery to the tissues of the groin from the first appearance of the abdominal wall. We shall see (p. 553) that we are dealing here with a structure of very ancient origin—one which is under the domination of sex hormones. At first the extension of the inguinal fold is represented merely by fine strands that traverse the tissue of the groin, but in later months increases in mass, and carries over it and in front of it, into the scrotum or labium majus, a process of the peritoneum and attenuated representatives of each stratum of the belly-wall (Fig. 494). The inguinal canal, the round ligament of the uterus and the gubernaculum testis are thus formed by the extension of the substance of the inguinal fold. From the stratum of muscular tissue which is found everywhere under the pelvic peritoneum, particularly around the genital cord, are formed the round ligament of the ovary, the muscular tissue in the utero-rectal (utero-sacral) ligaments and in the broad ligaments and also the outer muscular coat of the uterus.

Formation of Uterus and Vagina.—The parts of the Müllerian ducts lying side by side in the genital cord (Fig. 462) meet and unite early in

the 3rd month and by their fusion the uterus is formed and ultimately the vagina too. In all the members of the vertebrate series below and including the monotremes, the Müllerian ducts remain separate and open in the cloaca (Fig. 463, *A*). The process of fusion may be arrested at any point; it may cease when the upper vaginal segments have merged into each other—as in certain marsupials. Next, the septum between the lower or cervical parts of the uterine segments disappears; the human

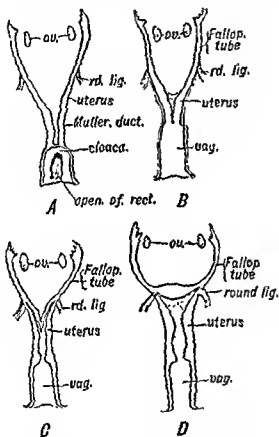


FIG 463. Evolution of the Human Form of Uterus.

A, from man in 1st month; B, from man in 2nd month; C, from man in 3rd month; D, from man in 4th month.

uterus then (2½ months) resembles that of higher mammals (carnivora, etc., Fig. 463, *C*). It may be arrested at this stage (uterus bicornis). Lastly the upper part of the septum disappears (3½ months, Fig. 464). The fundus, which is the last part to disappear, is quite well marked in the highest primates, is quite well marked in the human.

The musculature [21] appears in the wall of the uterus, vagina and tubes during the 4th month, the inner or circular, and the outer or longitudinal. Some time after the birth of the child the

the musculature of the uterus, and the distinction between the two primary layers becomes obliterated. Glands begin to form in the uterine mucosa during the 4th month of foetal life and a little later the cervix becomes differentiated from the vagina (Fig. 465). At this time,

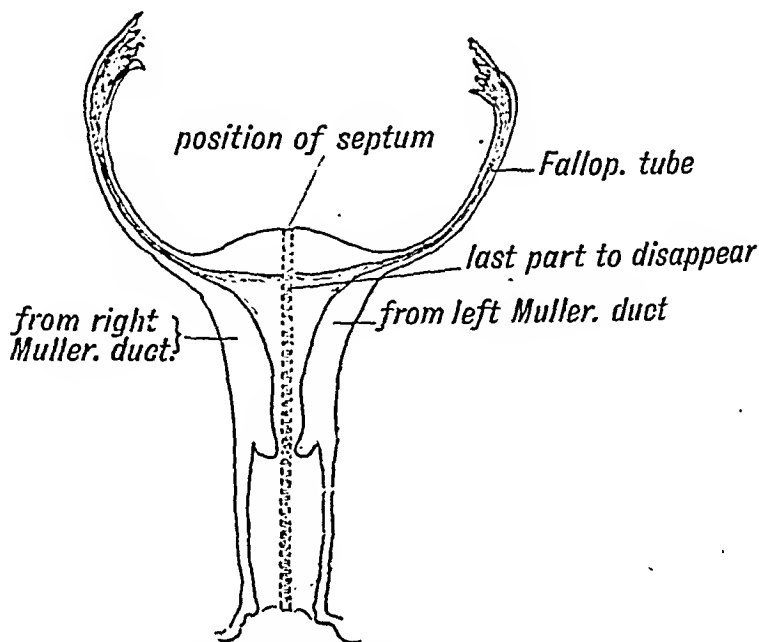


FIG. 464. Showing the bilateral origin of the Uterus and Vagina. The positions at which parts of the septum may persist are indicated along the mid-line.

too, the ovarian extremity of the Fallopian tube becomes wide and trumpet-shaped; the mucous membrane within it becomes plicated. The fimbriae are then formed by the extremities of the plicae growing

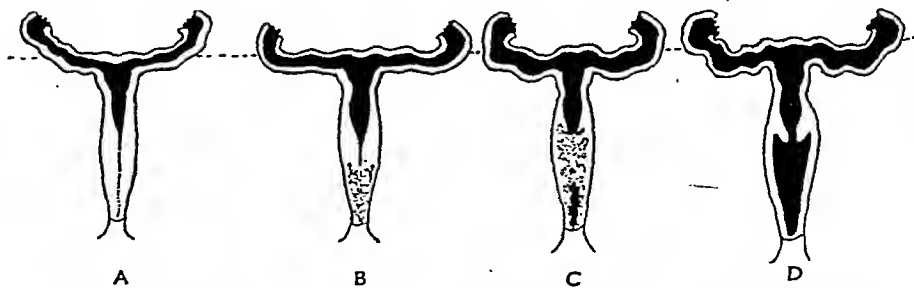


FIG. 465. Demarcation of the Vagina and Cervix from Body of the Uterus during the 4th month (A), 5th month (B), 6th month (C), and 7th month (D). (R. H. Hunter.)

out at the ostium abdominale. Secondary or accessory ostia may also be produced.

By the 7th month (Fig. 465) the foetal uterus is divided into two parts, the cervix or lower segment and body or upper segment. The lower segment or cervix forms then two-thirds of the uterus; its walls are thick and its upper part is lined by columnar non-ciliated epithelium,

containing racemose mucous glands. Its mucous membrane is arranged in palmate folds. The upper or uterine segment composes only a third of the uterus. It is lined by columnar epithelium, which becomes ciliated at the end of foetal life. At puberty the body of the uterus, instead of being half the size of the foetal cervix, becomes larger than it. The cervix takes no part in menstruation nor in containing the foetus; its true function is unknown. The external os is formed at the junction of the vaginal cords with the uterine segments of the Müllerian ducts; it becomes demarcated in the 5th month (Fig. 465). For some time after birth the body of the uterus actually undergoes a reduction in size [22]; growth does not become marked until the 7th year.

Metamorphosis of the Vagina.—About the middle of the 3rd month the lower ends of the Müllerian ducts of the human embryo undergo a remarkable metamorphosis, first fully described by Berry Hart and reinvestigated by Prof. Wood-Jones [23]. During the 4th, 5th and 6th months the human vagina is represented by an epithelial core or column (Fig. 465, *A*, *B*, *C*). The vaginal core, which is bilateral in nature, proliferates and expands until the 7th month, when the central mass breaks down and the cavity of the vagina is formed (*D*). There is still a question as to the origin of the vaginal epithelium. There are some who, like Prof. Wood-Jones, trace it to the Wolffian bulbs; there are others who derive it from the lining of the urogenital sinus; but the opinion which is best supported by evidence is that which derives it from the Müllerian bulbs (p. 517). If we accept the last-mentioned theory, then we must regard the vagina as a continuation of the Müllerian ducts. This much is certain; the epithelium which lines the developing vagina is highly susceptible to the action of oestrin; so too is the epithelium which lines the urogenital sinus [24].

Why should the vagina undergo this strange metamorphosis? It is a means of bringing down the terminations of the Müllerian ducts so that they may open on the vulval cleft (Fig. 466). In a female human foetus of the 3rd month these ducts open high up in the dorsal wall of the urogenital sinus, a position which is permanent in many mammals, such as the rabbit. In the metamorphosis of the vagina we are witnessing a means of transporting the end of the Müllerian tract to the vulval cleft, the urogenital sinus being greatly shortened until it forms merely part of the vulval cleft.

Atresia of the vagina results from a failure of the process of canaliculization. The bilateral elements of the vaginal cord may fail to fuse at one or more points, thus giving rise to septa within the vagina. Only the tip of the vaginal cord reaches and penetrates the wall of the urogenital sinus; hence a partial septum, the *hymen*, marks the opening of the

vagina into the urogenital sinus [25]. The extent to which the terminal septum breaks down varies widely; hence the numerous forms assumed by the hymen.

A remarkable example of the plasticity of the tissues of the genital

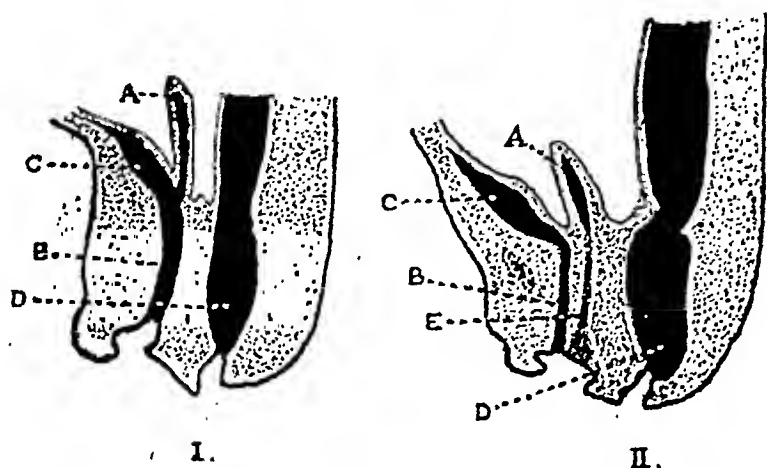


FIG. 466. Diagrams showing the Termination of the Vagina about the 9th week (I) and about the 13th week (II). (After Wood Jones.) A, Müllerian ducts (vagina and uterus); B, urogenital sinus; C, bladder; D, rectum; E, vagina represented by a cord of epithelium.

cord, with the formation of a new vaginal passage, is to be found in a discovery made by Prof. J. P. Hill [26]. In lower marsupials the vaginal segments of the Müllerian ducts are separable into two parts—upper, or

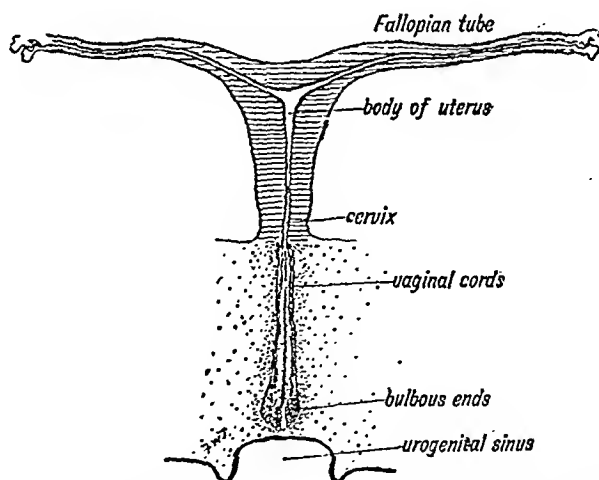


FIG. 467. Diagram illustrating the manner in which the Vaginal Cord or Plug is formed. (Wood Jones.)

cranial, which lie side by side and reach towards the cloaca (Fig. 468) lower, or caudal, which form lateral loops before terminating in the cloaca Hill found that the young are born by passing from the upper or medial segments into the cloaca by the formation of a new I ——— In hishe:

marsupials he found that the upper parts of the vaginal segments became fused to form a median vagina, and that the new passage to the cloaca was not temporary, as in lower marsupials, but permanent. In the foetus of the American opossum the greater part of the lateral vaginal canals is formed by upgrowths from the urogenital sinus (R. K. Burns). In monotremes, the Müllerian ducts have to serve only for the passage of unhatched ova, but with the evolution of gestation the ducts, which could convey ova, were unfitted for the transmission of young, and a new passage or median vagina was formed. The evidence is conclusive that there was a phase in human evolution when the Müllerian ducts

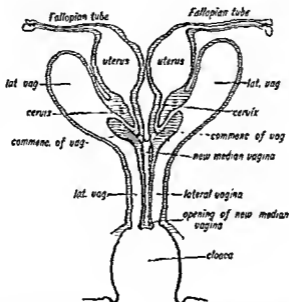


FIG 468 Diagram showing the arrangement of the Müllerian Duct in a Marsupial Mammal and the manner in which a New Vagina is formed for the passage of the young at birth (F. Wood Jones after J. P. Hill)

terminated in a cloaca; the metamorphosis of the vagina in the 4th and 5th months recalls a transformation of the same plastic nature as that which occurs in marsupials.

Müllerian Ducts in the Male.—In the male foetus of the 3rd month the Müllerian ducts are undergoing atrophy, the distinction between the testis and ovary being quite marked by this time, and the process of sexual differentiation recognizable on close examination. All that remain of the Müllerian ducts in the adult male are their fused terminal or vaginal segments forming the sinus *pocularis* or *uterus masculinus* in the prostate (Figs. 453, 469). Its depth is commonly about 3 or 4 mm., but occasionally such a form as is represented in Fig. 470 occurs and shows the real nature of the sinus *pocularis*. The vagina and uterus can be recognized in such cases. The *fimbriated* ends of the Müllerian ducts

persist as the sessile hydatids on the testicle (Fig. 453). The intermediate part of the tube disappears in the 3rd month and its site becomes greatly stretched during the descent of the testicle. A remnant of its upper end can be found in the sharp anterior border of the epididymis

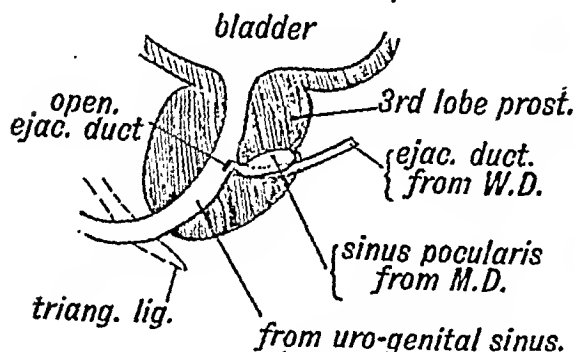


FIG. 469.

FIG. 469. A section of the Prostate showing the Remnants of the Lower Ends of the Müllerian Ducts in the Male.

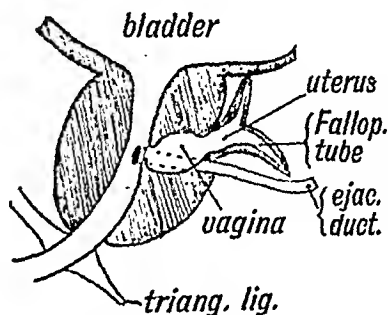


FIG. 470.

FIG. 470. A section of a Prostate showing an unusually developed Uterus Masculinus. (After Primrose.)

until quite a late period in foetal life. The mesosalpinx shrinks and completely disappears in the anterior border of the epididymis. In cases of imperfectly differentiated sex—so-called hermaphrodites—the Müllerian ducts assume the uterine form (see p. 559). Also they are sensitive to the action of oestrin (p. 521).

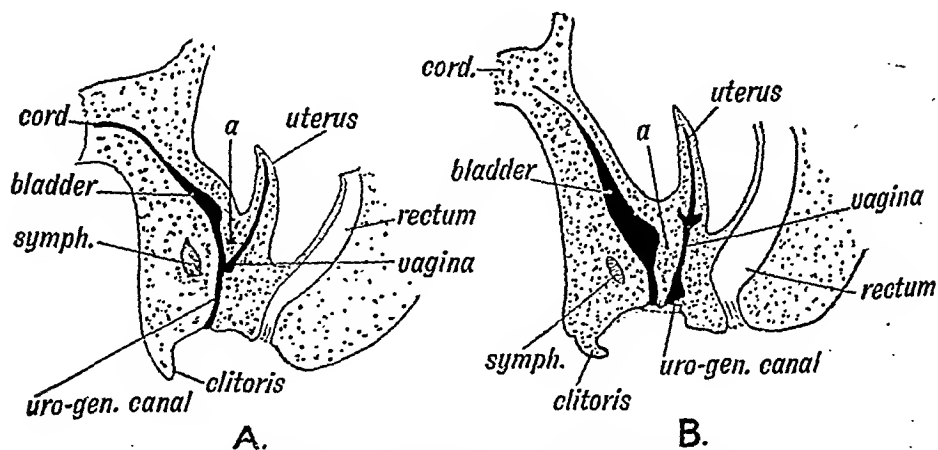


FIG. 471. Section showing the Urogenital Sinus.

A, in the 3rd-month female human foetus; B, in the 7th-month female human foetus; a, the vesico-vaginal septum.

Urogenital Sinus or Canal.—The Müllerian ducts open side by side into the ventral or urogenital part of the cloaca (Fig. 460), between and below the openings of the Wolffian ducts (Fig. 461). That part of the cloaca which serves as a common channel for bladder, Müllerian and Wolffian ducts is the urogenital sinus (Fig. 471, A, B). In the female foetus of

the 3rd month it is still well marked. In some mammals this passage-like sinus is retained. By the beginning of the 4th month in the female foetus (Fig. 471, B) it will be seen that the urogenital sinus has become

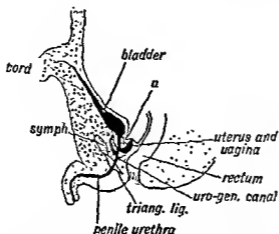


FIG. 472. Section showing the Urogenital Sinus in the Male Foetus. *a* indicates the part corresponding to the vesico-vaginal septum of the female. It is occupied by the 3rd lobe of the prostate.

shortened and opened out to form the floor of the pudendal or vulval cleft from the glans clitoris in front to the fossa navicularis behind, and thus the end of the Müllerian ducts (vagina) and urethra come to have

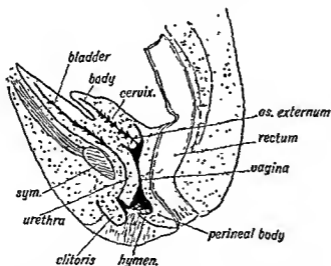


FIG. 473. A section to show the condition of the Vagina and Uterus at the 9th month of Foetal Life.

separate openings. The lining epithelium of the developing urogenital sinus is plastic in nature and is particularly sensitive to the action of sex hormones, especially in the female to that of oestrin. In the male (Fig. 472) the early foetal form is retained, and the urogenital sinus

becomes that part of the urethra which extends from the sinus pocularis in the prostate to the fossa navicularis in the glans penis. The female urethra corresponds to the prostatic part above the opening of the sinus pocularis of the male urethra.

The **Hymen** is formed at the junction of the vagina with the urogenital sinus, being covered on its outer surface by epithelium derived from the urogenital sinus and on its deep surface by epithelium of the vaginal cord [27]. Usually at one point on the hymen, but occasionally at several, the epithelial coverings fuse and break down, leading to one or more perforations. On the other hand, the vaginal cords may not reach the urogenital sinus, the hymen being then imperforate. In reptiles, as in the human embryo, the part of the urogenital sinus into which the Müllerian and Wolffian ducts open, forms the trigone of the bladder (see p. 544). In such animals the hymen prevents the reflux of urine into the Müllerian ducts.

NOTES AND REFERENCES

[1] My account of the evolution of the urogenital system is based on observations by the following authors: Felix, W., Keibel and Mall's *Manual of Human Embryology*, 1912, vol. 2; Lewis, F. T., *Amer. Jour. Anat.*, 1919, 26, 423; Gray, P., *Quart. Jour. Mic. Sc.*, 1930, 73, 507 (development in amphibia).

[2] For development of the Wolffian body, see Shikunami, J., *Contrib. Emb.*, 1926, 17, 49; Frazer, Eliz., *Jour. Anat.*, 1920, 54, 287; Kampmeier, O. F., *Anat. Rec.*, 1926, 33, 115; Altschule, M. D., *ibid.*, 1930, 46, 81; Gersh, I., *Contrib. Emb.*, 1937, 26, 35 (as functional kidney); Wreite, M., *Anat. Anz.*, 1934, 77, 273.

[3] For recent papers on pronephros, see Heuser, C., *Contrib. Emb.*, 1930, 22, 140; Weinberg, E., *Anat. Rec.*, 1929, 41, 373; O'Connor, R. J., *Jour. Anat.*, 1939, 73, 145; 1940, 74, 301 (experiments on pronephric duct in amphibia); Armstrong, P. B., *Amer. Jour. Anat.*, 1932, 51, 157 (in *Fundulus*).

[4] Duthie, G. M., *Jour. Anat.*, 1925, 59, 410; Fleming, A., *ibid.*, 1927, 61, 232; Wilkerson, W. V., *Anat. Rec.*, 1923, 26, 75 (rete testis in female); Wilson, K. M., *Contrib. Emb.*, 1926, 17, 69; 1926, 18, 23 (rete testis); Grünwald, P., *Zeitsch. Anat. Entwickl.*, 1934, 103, 1, 259; Wallart, J., *Archiv. Biol.*, 1934, 45, 47.

[5] Doran and Keith, *Jour. Obstet. Gynaec.*, 1910, 18, 246; Müller, J. H., *Ann. d'Anat. Path.*, 1934, 11, 483.

[6] Wilson, K. M., see under note [4]; Frazer, J. E., *Manual of Embryology*, 1940.

[7] Allen, B. M., *Amer. Jour. Anat.*, 1906, 5, 79; Wilson, K. M., see note [4]; Simkins, C. S., *ibid.*, 1928, 41, 249; Brambell, F. W. R., *Proc. Roy. Soc.*, 1927, 102 (B), 206 (rete testis of mouse); Burns, R. K., *Anat. Rec.*, 1941, 79, 84.

[8] See references to Doran and Keith, note [5]; to Duthie and to Wilkerson, note [4].

[9] For development of kidneys, see Kampmeier, O. F., reference in note [2]; Huber, G. C., *Amer. Jour. Anat.*, 1906, 4 (suppl.); Seevers, C. H., *Anat. Rec.*, 1932, 54, 218 (organizing influence of ureteric bud); Mijsberg, A. W., *Anat. Anz.*, 71, 249 (suppl.); Fuchs, F., *Zeitsch. Anat. Entwickl.*, 1933, 101, 746 (formation of renal calyces); Heidenhain, M., *Synthetische Morphologie der Niere*, 1937; Graham

[24] Dr. Baxter (note [19]) observed no shortening in the urogenital sinus in the rabbit during vaginal metamorphosis. The upper vaginal core he derived from the Mullerian ducts, the lower from the Wolffian. Dr. Koff (note [19]) derives the core

from a Müllerian source ; Dr. Vilas (note [19]) from the epithelium of the urogenital sinus ; Dr. Burns (note [19]) from the proctodaeal epithelium.

[25] For development of hymen, see references in notes [19, [24].

[26] Hill, J. P., *Proc. Linn. Soc. N.S.W.*, March 20, 1899, August 27, 1900.

[27] Afterwards the lower surface of the hymen becomes covered by vaginal epithelium (R. H. Hunter).

CHAPTER XXVI

UROGENITAL SYSTEM (continued)

Evolution of the Penis.—The transformation of the mesonephros to form an adjunct of the genital system of the male, which we have been considering, is of ancient origin, but those remarkable changes which

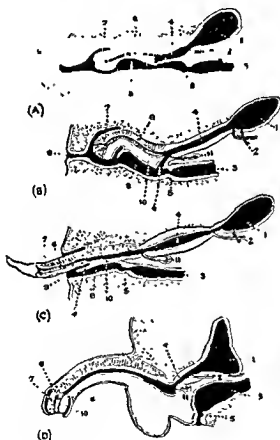


FIG. 474. Drawing in the text.

are seen to occur in the perineum of the human embryo, and which we are now going to consider, represent a much later evolutionary movement. Even in the lowest mammals, monotremes and marsupials, the rectum and urogenital ducts end in a common terminal passage—the cloaca (Fig. 474, B). In the human embryo, until the 7th week of develop-

ment, this is also the case ; but about the beginning of this week, when the embryo is 12 mm. long, changes occur which separate the rectal and urinary passages. These changes have been occasioned by the evolution of an external or extra-cloacal penis [1]. In Fig. 474 stages in the evolution of the penis are represented. In the tortoise the penis lies on the pubic or ventral wall of the cloaca ; during copulation the cloaca is partially everted and the open groove of the penis is converted into a canal by the application of the dorsal or opposite wall of the cloaca. In *Echidna*, a primitive mammal, the penis is still intra-cloacal ; its groove is converted into a canal, except posteriorly, where there is still a communication between the urogenital and cloacal passages—which represents the primitive urogenital orifice, for the penile canal is a new passage (Fig. 474, *B*, 6). In marsupials (Fig. 474, *C*) the penis is still partially intra-cloacal, but the primitive urogenital orifice is closed and the urogenital passage is now separated from that which serves for the faeces. In man the penis, as in all primates, has been permanently extruded and is now completely extra-cloacal, and a perineal body separates the rectal orifice from the urogenital passage. The *metamorphosis of the cloaca* is thus a result of the evolution of the penis. The external penis with a complete penile urethra appears with the evolution of a vagina, uterus and the intrauterine nourishment of the young. The cloacal passage is seen in oviparous mammals ; in viviparous mammals the penis is evolved as an intromittent organ, and the urogenital passage is separated from that of the rectum.

Twofold Origin of the Cloaca.—The primitive cloaca, as represented in Fig. 474, *A*, is of double origin, the deeper part in which the rectum and urogenital sinus end is derived from the hind-gut and is thus of endodermal origin. The more superficial part, enclosed by the cloacal lips, arises as a perineal depression and is thus of ectodermal origin. Students of embryology, however, when they speak of cloaca have in mind only the part derived from the hind-gut—the endodermal cloaca. The development of the perineal region cannot be understood unless it is remembered that both ectodermal and endodermal elements play a part in fashioning the anal and vulval orifices of the human embryo.

Cloaca of the Embryo.—Having in the previous chapter traced the origin and fate of the genital ducts, it is now necessary to follow the changes which are undergone by the cloaca—the common vent for the rectum and genital passages [2]. We have already seen that the cloaca appears early in the 4th week (Fig. 322), its precocious origin being due to the fact that it gives rise to the allantois, by means of which the chorionic circulation is established. Thus in the 5th week (Fig. 478, *A*), the cloaca forms a relatively large cavity, into which open the rectum

and allantois, while the Wolffian duct is also establishing a communication with its more ventral part. At this time the outline of the cloaca, as seen on making a median section of the embryo, is triangular in shape; its dorsal wall follows the curve of the notochord to the point of the tail; a large part of its ventral wall is formed by the cloacal membrane (Fig. 478, A), which is composed of only the two primitive layers, the endoderm which lines the cloaca and the ectoderm which covers the embryo. It will be remembered (see p. 55) that the hinder end of the embryonic body is produced on each side of the primitive streak. The cloacal membrane represents the hindmost part of the primitive streak, which has been thrust into a ventral position by the outgrowth of the tail (Fig. 475). During the 4th week and also for the greater part of the 5th, the hinder end of the body represents its growing end; it may be spoken

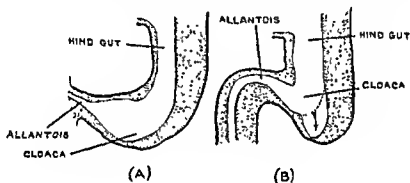


FIG. 478. (A) 4th Week, from the Hind end of the 4th week. (B) 5th Week.

of as the *rump bud* (Fig. 45, p. 55). As the bud grows and differentiates it carries backwards not only the spinal cord, vertebrae and spinal muscles but also the cloaca. In this way it comes about that the hinder apex of the cloaca extends beneath the tail and behind the cloacal membrane and forms that transitory structure known as the *tail gut* (Fig. 478). In the 4th week the cloaca has no perineal opening; this opening is first established near the end of the 2nd month by an absorption of the cloacal membrane. We have seen that the cloacal membrane, at a very early stage of development, extends on to the wall (ventral) of the allantois (p. 54).

Evolution of Cloacal Structures.—To understand the significance of the changes undergone by the cloaca in the human embryo, one must have a clear conception of the various evolutionary stages known to the comparative anatomist. We have already seen that some of these changes are related to the differentiation of an external penis; it is now necessary

to see how the cloaca becomes modified to assume its mammalian and human form. The essential stages are represented in Fig. 476; in the frog (*A*) the cloaca receives the bladder, rectum and Wolffian ducts, the

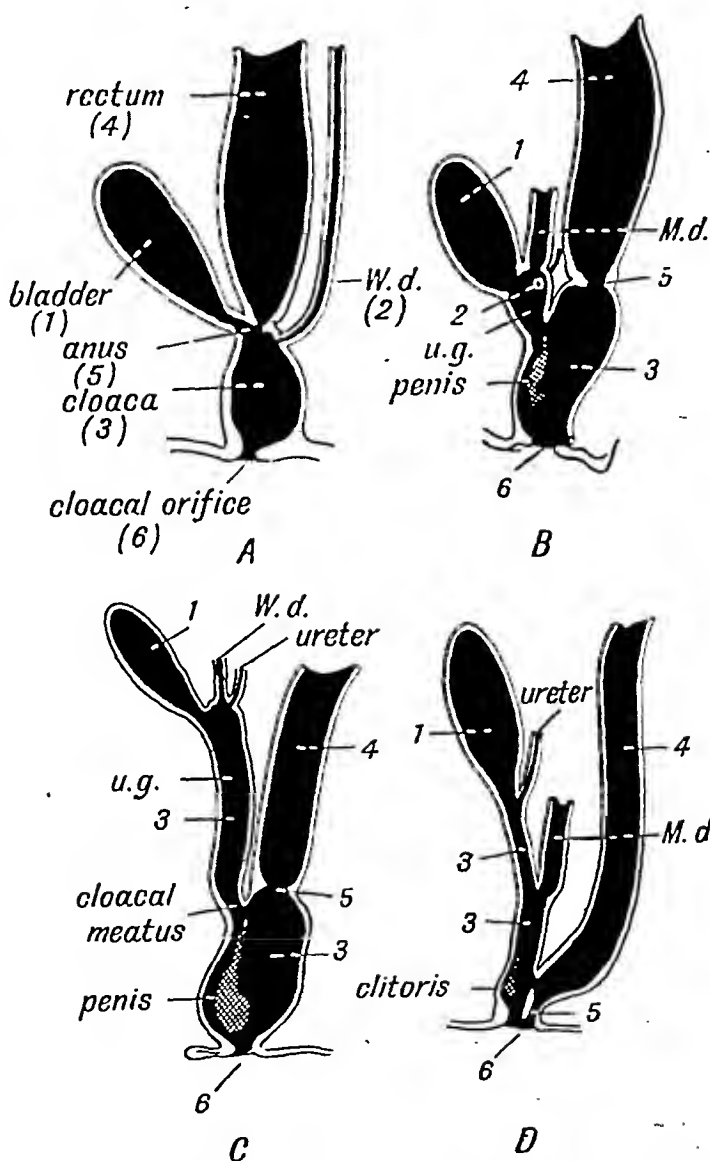


FIG. 476. Diagrams to show the manner in which the Cloaca is modified and the Termination of the Rectum transferred from the Cloaca to the Perineum in Higher Vertebrates. *A*, the amphibian form; 1, bladder; 2, Wolffian duct (ureter and vas); 3, cloaca; 4, rectum; 5, intra-cloacal anus; 6, cloacal orifice; *M.D.*, Müllerian duct; *B*, form found in the tortoise; *C*, form in monotremes; *D*, form found in female marsupial.

ducts opening distal to the rectum, being thus nearer the cloacal vent. In the tortoise (*B*) the rectum has passed distal to the Wolffian ducts, which now open with the bladder into a common part of the cloaca—the urogenital sinus (Fig. 476, *B*, *u.g.*). In the lowest mammals, monotremes (*C*), the urogenital sinus has become elongated and assumed

the form of a urethra; the ureters are now severed from the Wolffian ducts, but still open on the floor of the urogenital sinus; the urine thus has to pass across the urogenital sinus to reach the bladder. In marsupials (*D*) a further stage is reached; the opening of the rectum has migrated backwards on the posterior wall of the cloaca until it almost reaches the perineum. This posterior migration of the rectal opening (anus) is already seen in *Echidna* (*C*), where the urogenital sinus—which represents the proximal part of the cloaca—has assumed a considerable length. Thus in the evolution of mammals we see that the rectum migrates backwards until its vent or anus almost reaches the surface of the perineum, leaving the greater part of the cloaca as the urogenital sinus.

Ectodermal Cloaca.—The forms of cloaca depicted in Fig. 476 are not

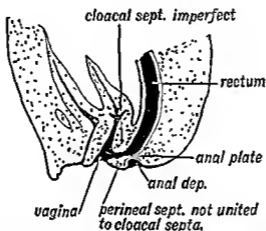


FIG. 477. Case of a Female Child in which the Rectum opened on the Vestibule while the Normal Anus remains closed by the Anal Plate. The opening on the vestibule represents the ancient cloacal orifice of the rectum.

entirely derived from the gut or endodermal cloaca, which is seen in the human embryo. The terminal or superficial part is derived from a *cloacal depression* or pit formed on the perineum, and lined by epithelium derived from the ectoderm. The glans of the penis and also of the clitoris are formed in the ectodermal part: the rest of the penis and clitoris is developed in the endodermal part (Fig. 474). We have already seen how the urethral groove of the cloacal penis becomes closed off as a separate channel by the union of two vestibular folds—*seminal guides*. Prof. Wood-Jones has named them—the penile urethra being thus enclosed. In *Echidna* (Fig. 474, *B*) one sees that the urethra is made up of two parts—an upper derived from the urogenital sinus and a lower or penile from the channel enclosed by the lateral vestibular folds. At the junction of these two parts of the urethra there remains a communication between the urogenital sinus and the cloaca which

represents the primitive opening of the urogenital sinus (Fig. 474, *B*). In marsupials the primary urethra (urogenital sinus) and secondary or penile urethra have united by the closure of the primitive opening of the urogenital sinus, and thus the passage for the urine and semen becomes completely separated from that for the faeces. The rectum is

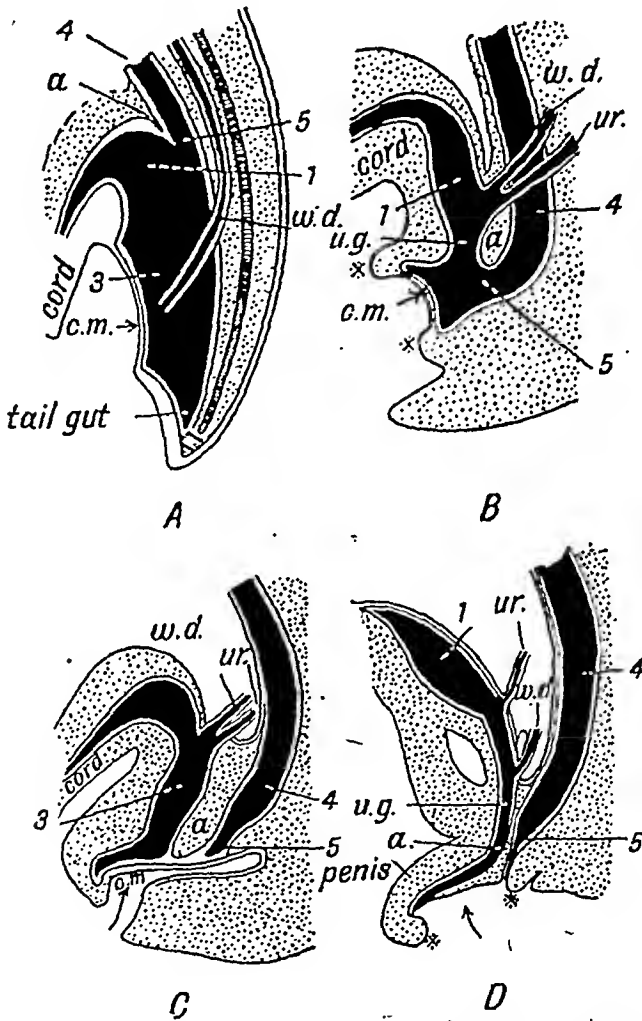


FIG. 478. Showing the manner in which the Rectum becomes separated from the Urogenital Sinus (endodermal cloaca) during development of the Human Embryo. *A*, Human embryo of 5th week, 4 mm. long (after Keibel). *B*, From human embryo of 6th week, 11 mm. long (after Keibel). *C* and *D*, Later stages (7th and 9th weeks) of development: 1, bladder; 2, Wolffian duct (ureter and vas); 3, endodermal cloaca; 4, rectum; 5, anus; *C.M.*, cloacal membrane; *U.G.*, urogenital sinus; *a*, urorectal septum; ** limit of the perineal depression (ectodermal cloaca).

detached from the urogenital sinus and opens directly into the ectodermal cloaca.

Differentiation of the Human Cloaca.—We are now in a position to interpret the changes which occur in the human cloaca during the 5th, 6th and 7th weeks of development (Fig. 478). In the 5th week the rectum ends proximal to the Wolffian duct as in the frog; in the 6th

week the cloacal orifice of the rectum has moved backwards, leaving the proximal part of the cloaca as the urogenital sinus, a condition similar to that seen in *Echidna* (Fig. 476, *C*). As in that animal, the Wolffian ducts and ureters open close together in the sinus. During this migratory period the embryonic rectum is ensheathed within rapidly growing plastic tissue; the movement is one of growth [3]. The appearance presented by the backward migration of the rectal orifice is exactly the same as if the cloaca had been divided into rectal and urogenital cavities by the urorectal septum marked "*a*" in Fig. 478, *B, C*. In the 7th week (Fig. 478, *C*) the rectum, having reached the anal part of the cloacal membrane, forms a new opening, the former opening into the cloaca becoming closed (Fig. 478, *D*). But as we have seen (Fig. 477), the cloacal anus may persist and the true anus fail to form.

Here we must note an important change which takes place in the ventral wall of bladder and urogenital sinus between the 5th and 6th weeks (Fig. 478, *A, B*). In the 5th week this ventral wall is formed by the cloacal membrane; in the 6th the membrane is invaded from the right and from the left by ventral mesoderm in which, at a much later date, the symphysis will be formed. Already in the 6th week (Fig. 478, *B*) the ventral mesoderm is growing out into an eminence (the genital eminence) at the ventral end of the ectodermal cloaca, carrying with it an extension of the urogenital sinus. In the two following weeks the ventral extension of the urogenital sinus becomes more and more marked. The ventral or forward extension of the sinus forms the lining for the penile urethra of the male and the covering for the vestibule in the female. The cloacal membrane on the floor of this penile extension of the cloaca breaks down towards the end of the 7th week and the urogenital sinus thus presents a fissure-like opening on the perineum. The fissure corresponds to the groove on the open urethra of the tortoise (Fig. 476, *A*).

On each side of the perineal fissure, which opens into the floor of the urogenital sinus, there appears, towards the end of the 7th week, a fold, the *inner genital fold*, forming the lateral lip of the cloacal or urogenital orifice [4]. It is important to note how these folds end behind. They end in the lower margin of the urorectal septum, which at this time (7th week) has reached the perineum (Fig. 478, *C*). The posterior ends of the right and left folds unite to form a commissure or fourchette. Thus the orifice of the urogenital sinus in the perineum is bounded behind and laterally by the inner genital folds and anteriorly by the genital eminence on which they end. As the genital eminence or tubercle grows forward, the orifice of the sinus is also advanced; in this way the floor of the male urethra is formed. If the backward migration

of the rectum is arrested, then the ancient cloacal anus is retained, opening in the urethra of the male or vestibule of the female (Figs. 477, 479). It will thus be seen that in the human embryo the rectal orifice migrates backwards until it opens in the posterior part of the perineal depression (ectodermal cloaca), leaving the whole of the endodermal cloaca of the embryo as a urogenital passage or urethra. All these changes take place during the latter part of the 2nd month.

Formation of the Perineum.—By the end of the 7th week the termination of the foetal rectum has reached the hinder end of the external-cloaca and, at the same time, the urorectal septum (Fig. 478, *C, a*) comes in contact and fuses with the cloacal membrane. We have seen how the lateral mesoderm invades the anterior part of the cloacal membrane to

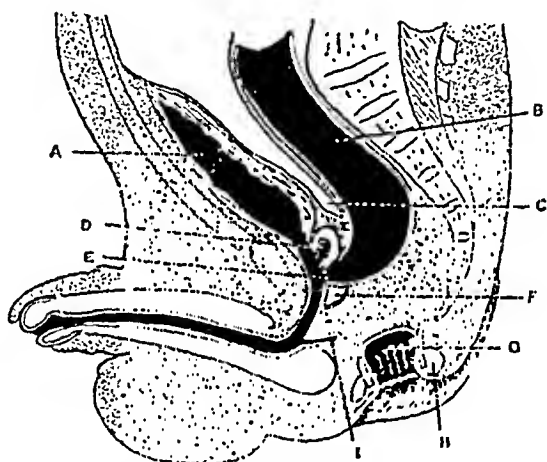


FIG. 479. Section of Pelvis of a Male Child showing the Rectum ending in the Prostatic Part of the Urethra. *A*, bladder; *B*, rectum; *C*, recto-vesical pouch; *D*, uterus masculinus; *E*, intra-cloacal anus; *F*, prostate; *G*, anal depression (ectodermal); *H*, external and internal sphincters; *I*, Cowper's gland.

form the pubic region and genital eminence. There is a similar mesodermal invasion of the lower margin of the urorectal septum and of the cloacal membrane with which it has fused, and thus the hinder part of the external cloaca, with its plug of ectoderm, is cut off by the formation of the perineal body (Fig. 478, *D*).

Malformations of Rectum and Anus.—In Fig. 479 one of the commoner malformations of the rectum is depicted in a male child. The rectum is seen to terminate in the urethra just distal to the sinus pocularis, which represents the uterus and vagina of the female. The rectum has retained its ancient cloacal orifice, or we may say there has been a failure in the migration of this orifice. Nevertheless a normal anal canal has been formed, showing that the developmental tissues in the posterior part of the external cloaca can act independently of the rectal tissues, for one might conceive that the one acted on the other as an inducing agent.

Nor has the arrest of descent of the rectal termination interfered with a normal formation of the perineal body.

In Figs. 477, 480 an exactly similar condition is represented in female infants. The rectum opens in the male below the orifice of the uterus masculinus, in the female at a corresponding point below the orifice of the vagina. The urorectal septum and inner genital folds in the female form merely the perineal body, which separates the terminal part of the rectum from the vulva; in the male they form the floor of the urethra and perineum from the sinus pocularis to the lacuna magna in the glans penis. The terminal part of the male urethra, as we shall see presently, has a separate origin. The downward migration of the vaginal orifice in women brings the cloacal opening of the rectum into



FIG 480 Section of Pelvis of Female Infant, showing the Rectum opening into the Navicular Fossa of the Vulva. *A*, bladder, *B*, rectum, *C*, recto-uterine fold, *D*, symphysis, *E*, vulval anus, *F*, cervix; *G*, anal depression (rarely present when rectum opens in vulva); *H*, urethra, *I*, clitoris, *K*, hymen, *L*, Labium minus

the vulva—the roof of the vulval cleft being a derivative of the urogenital sinus. In many cases of imperforate anus (Fig. 481) the cloacal anus is closed and the rectum terminates an inch or more from the anal depression. In other cases merely a thin septum separates the anal depression from the termination of the rectum. In extreme cases, which are by no means rare, no anal depression is formed and the sacral part of the rectum is absent.

There is some confusion as to how much of the anal canal is formed from rectum and how much from anal depression. As may be seen from Figs. 479 and 480, certain vertical folds are formed in the wall of the anal depression. At the upper end of these anal folds, which are scarcely recognizable in the fully developed anal canal, are developed certain valve-like folds of mucous membrane, the *anal valves*. The interval

sphincter is developed round the lowest part of the endodermal rectum. Above the valves are the well-marked columns of Morgagni formed in the rectum. The valves mark the junction of the rectum with the anal depression [5].

External Genital Organs and Perineum.—That the interpretation just given of the embryological parts entering into the formation of the rectum and urethra is right is seen when the development of the external genital organs is traced. The stages in the development of the human urethra, penis and scrotum during the latter part of the 2nd month and earlier part of the 3rd are shown in Fig. 482. Stage I represents the condition seen in the perineum about the end of the 8th week [6]. The circular fold *A*—cloacal fold [7] it may be named, represents the opening or margin of the primitive (ectodermal) cloaca. Within its

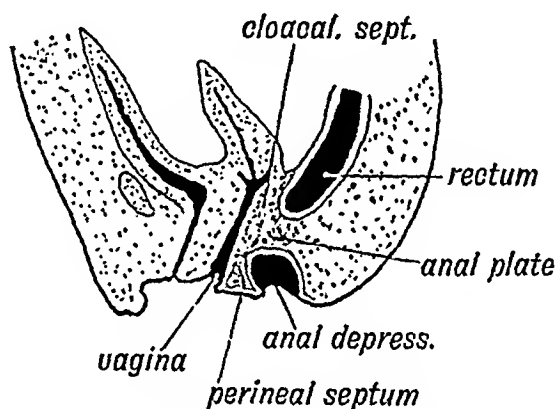


FIG. 481. A case of Imperforate Anus in which the Rectum has been arrested in its migration from the Cloaca to the Perineum.

anterior or pubic fornix is rising up the genital eminence to form the penis or clitoris—according to sex, for at this time the external parts of both sexes are alike, although the ovary is being differentiated from the testicle. There is a groove or furrow on the under or cloacal aspect of the genital eminence, as on the cloacal penis of the tortoise; it represents the roof of the penile urethra, and leads backwards to the urogenital sinus. The folds at each side of the furrow (*a, a*) are the vestibular or *inner genital folds* which form the penile urethra in *Echidna*. In Stage II (Fig. 482), reached during the 9th week, two further changes are seen in progress. The inner genital folds (*a, a*) are now united behind in the urorectal septum, thus helping to separate the anal part of the ectodermal cloaca (perineal depression), in which the rectum now terminates, from the anterior urogenital part. The cloacal or outer genital folds (*A, A*) are still well marked, but it is apparent that the genital eminence and its attached folds are being extruded from the cloaca. In Stage III,

reached by the end of the 9th week, a condition is represented which is common to both male and female foetuses.

In Stage II the anus still lies within the cloacal folds ; in Stage III it protrudes and is being separated from the urogenital orifice by the formation of the perineal body. In Stage III the inner genital folds are seen (Fig. 482, III) to meet behind in the perineal body, where their free margin forms a semilunar fold—the primitive fourchette. Anteriorly

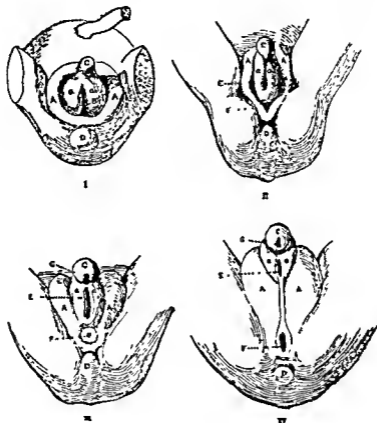


FIG. 482. Development of the urogenital system in a foetus.

the folds unite on the perineal aspect of the glans. Between the folds opens the penile urethra ; the opening between the folds is the orifice of the urogenital sinus ; it represents the primitive meatus of the penile urethra. On the under or perineal aspect of the glans a depression (the phallic groove) packed with an ectodermal plug is also present ; it forms the part of the urethra within the glans. Stage IV represents a condition peculiar to the male. A median raphe or suture is now seen extending from the anus behind to terminate anteriorly in the inner genital folds.

The orifice of the urogenital sinus (the part which forms the male urethra) has grown forwards and is now well advanced towards the glans penis. The median perineal raphe is caused by a fusion of the peculiar tissues of the cloacal or outer genital folds. The outer folds do not grow over and submerge the inner and so meet in the mid line. What happens is this: the mesoderm of the outer folds invades the fourchette or commissure in which the inner genital lips meet behind. As the fourchette is advanced towards the glans the invasion from right and left outer folds becomes more extensive; the line along which the invading tissues meet is marked by the median raphe, which in Fig. 482, IV, is seen to extend from the anus behind to the orifice of the urethra in front.

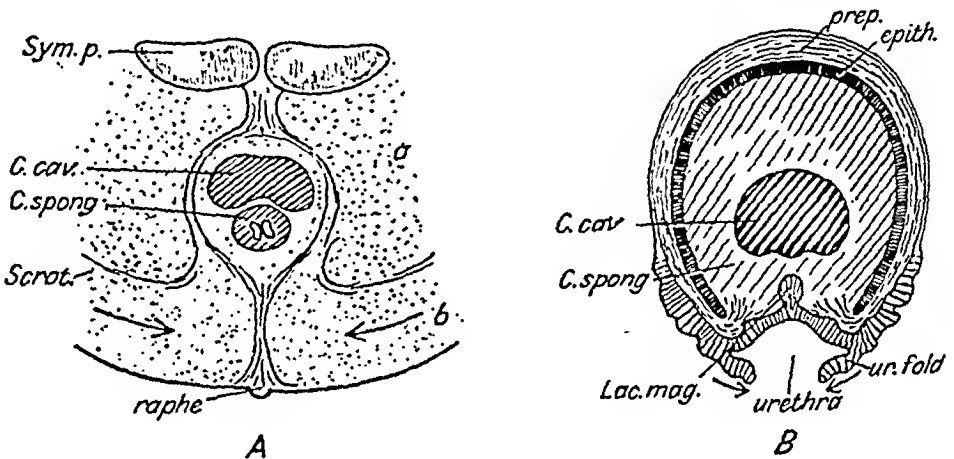


FIG. 483.

- A. A coronal section of the Scrotum of a Male Foetus of 3 months to show the manner in which the Median Raphe is formed. (Moszkowicz.) The arrows show the direction taken by the invading mesoderm. *a*, deep scrotal tissue; *b*, superficial tissue; *Sym. p.*, symphysis pubis; *C. cav.*, corpus cavernosum; *C. spong.*, corpus spongiosum; *Scrot.*, scrotum.
- B. Coronal section of the Glans Penis and Prepuce of a Male Foetus of 10 weeks. (Popper.) *ur. fold*, urethral fold (the arrows show direction of their union); *Lac. mag.*, lacuna magna; *epith.*, epithelium between glans and prepuce.

Out of the outer folds, fused in the manner just described, is formed the scrotum. There is no such invasion and fusion in the female and hence there is no median raphe. In the female the outer folds remain apart and form the labia majora [8].

By the end of the 3rd month the process of union which gives rise to the perineal raphe extends to the glans, and in this way the primitive meatus is closed, the terminal parts of the vestibular folds (urethral folds, Fig. 483, *B*) forming the fraenum of the prepuce. Thus the anterior parts of the vestibular folds unite right up to the fraenum of the prepuce, and enclose the male urethra. In Stage IV (Fig. 482) the margins of the phallic groove on the glans have united; the plug of epithelium within the groove breaks down. In this way the urethra is completed and a meatus established on the glans. In Stage IV the preputial

hood of skin is seen in process of formation. It is directly continuous with the anterior ends of the folds surrounding the primary meatus. It does not rise up as a free fold; the epithelium on the deep surface of the hood adheres to that on the glans, and hence when the glans is fully formed in the 4th month, the prepuce is tightly bound to it until a week after birth [9].

Hypospadias.—It is not unusual to see cases in which the process of urethral development has been arrested. In the female a complete arrest in the formation of the penile urethra is normal; in individuals with imperfect differentiation of sexual glands (usually imperfect males) the process is also arrested at an indifferent stage (Fig. 482, III). Fig. 484 represents three conditions of hypospadias due to arrest of development at the terminal stage. In *A* the phallic groove is unclosed; the urethra opens at the primary meatus; the folds bounding the meatus

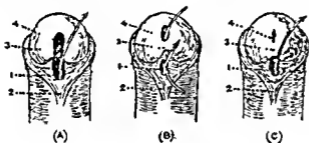


FIG. 484. Three conditions of hypospadias due to arrest of development at the terminal stage.

represent the anterior ends of the vestibular folds. In *B* the primitive meatus is unclosed, but the phallic groove is converted into a canal; in *C*, the commonest type, the primitive meatus is open and the phallic groove has remained uncanceled [10].

External Genitals of the Female.—In the female the parts retain closely the early foetal form represented in Fig. 485. The genital tubercle becomes the glans clitoris. In the genital eminence—of which the tubercle is merely the summit—the corpora cavernosa develop. The vestibular or inner genital folds form the *labia minora*, the prepuce and fraenum. By the junction of the inner genital folds within the urogenital depression behind, the *fourchette* is formed. Thus the opening into the urogenital sinus (primitive meatus) is bounded by the fourchette, labia minora and fraenum of the prepuce. In the lateral folds, or labia minora, are developed the bulbs of the vestibule. After the 3rd month the external genital (cloacal) folds become prominent around the urogenital depression and form the labia majora. The tissue within them

is derived from the "pubic apron" (see p. 553). They are united above the clitoris and form the mons veneris. Their posterior extremities fade away posteriorly (Fig. 482). After the 3rd month the external genital parts undergo a change directly opposite to that which takes place in the male. The primary meatus and penile urethra open up and form the vestibule, into which open urethra and vagina. When we come to consider the case of those individuals in whom the sexual organs are imperfectly differentiated we shall see that in their development all structures concerned in reproduction are dominated by the male and female hormones, the final form being determined by which of these two hormones is dominant [11].

External Genitals of the Male.—In the male, at the end of the 2nd month, the inner genital folds corresponding to the fourchette and labia minora grow forwards as a crescentic shelf, thus closing the urogenital

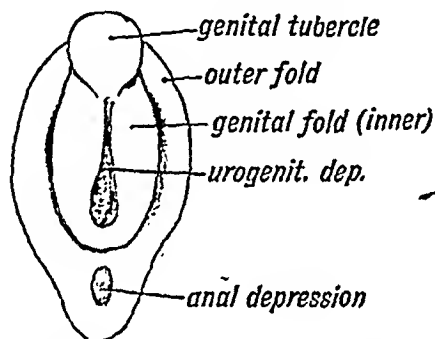


FIG. 485. Diagram showing the indifferent stage in the development of the External Genitals with the terms usually applied. The outer fold represents the cloacal or outer genital fold; the inner genital fold the anterior parts of the vestibular fold; the urogenital depression or cleft, the primary meatus (see Fig. 482).

cleft and forming the floor of the penile urethra [12]. While the floor of the penile urethra is formed thus, its roof, corresponding to the vestibule of the female, is derived from the forward prolongation of the cloaca (see Fig. 478). The erectile tissue in the inner genital folds, which becomes included in the bulbs of the vestibule in the female, is incorporated in the corpus spongiosum in the male. The corpora cavernosa are formed in the genital eminence. The anterior part of the corpus spongiosum is formed separately in the apical part (glans) of the genital eminence. The corpora cavernosa are developed by the enlargement of capillary vessels of the body of the genital eminence during the 4th month. The part of the urethra within the glans is the last part to be formed, and its development, as we have seen, is peculiar (p. 540). The part of the urethra within the glans becomes canaliculized a short time before birth. The fossa navicularis and lacuna magna occur at the junction of the part of the urethra formed in the glans and the part formed from the urogenital sinus [13].

The *scrotum* is formed during the 3rd month by the union of the tissues contained in the external genital folds (labia majora of the female); the raphe which marks this union extends from the fraenum of the prepuce in front to the anterior margin of the anus behind (see p. 540, Fig. 482, IV).

Perineal Muscles.—From what has been said regarding the cloaca, the evolution of the muscles of the perineum from the sphincter of the cloaca will be readily understood. The sphincter in cloacal vertebrates surrounds the part of the cloaca (perineal depression) formed from ectoderm; it is a striated muscle. At the end of the 2nd month this muscle is apparent in the cloacal fold of the human foetus (Fig. 486, A). It is at this time, too, that the perineal body is formed in front of the anus by a bilateral invasion of the mesoderm; with the invasion the

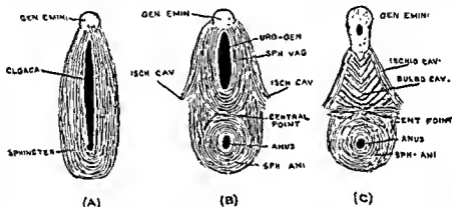


FIG 486 Stages in the Evolution of the Perineal Musculature. (After Popowsky.)
A, sphincter of the cloaca in the 2nd month; B, its division at the beginning of the 3rd month; C, its condition in the male foetus at the end of the 3rd month

cloacal sphincter becomes divided into anal and urogenital parts (Fig. 486, B) [14]. The sphincters of the urogenital passage and anus fuse in the perineal body. A part of the urogenital sphincter obtains an attachment to the ischium and forms the ischio-cavernosus (erector penis); another strand, the transversus perinei. With the formation of the urethra in the male, the sphincter of the urogenital passage is carried forwards on the bulb and forms the bulbo-cavernosus; in the female it remains as the sphincter vaginae. A deeper and older part surrounds the upper part of the urogenital sinus, and becomes the constrictor urethrae (see p. 545).

Origin of the Bladder.—In amphibians the bladder is a diverticulum of the cloaca. In the embryos of reptiles, birds and mammals its apical part undergoes a marvellous transformation during development, to form the allantois; part lies outside the body and is lost at birth, part remains within the body to form the urachus and all the bladder except

the trigone. By a downward migration of the orifices of the Wolffian and Müllerian ducts, the upper part of the urogenital sinus, retaining the insertion of the ureters, becomes the trigone of the bladder and supra-genital part of the urethra [15].

Urachus.—When the body-stalk becomes elongated in the formation of the umbilical cord, the part of the allantoic cavity within it is obliterated. The part of the allantois within the abdomen, stretching from the umbilicus to the apex of the bladder, becomes the urachus, a fibrous cord, in which all trace of the allantoic cavity is usually lost. Occasionally traces of the cavity may remain and form *urachal cysts* [16], or it may remain open throughout, so that urine escapes from the bladder by a fistula at the umbilicus. The urachus lies behind the linea alba,

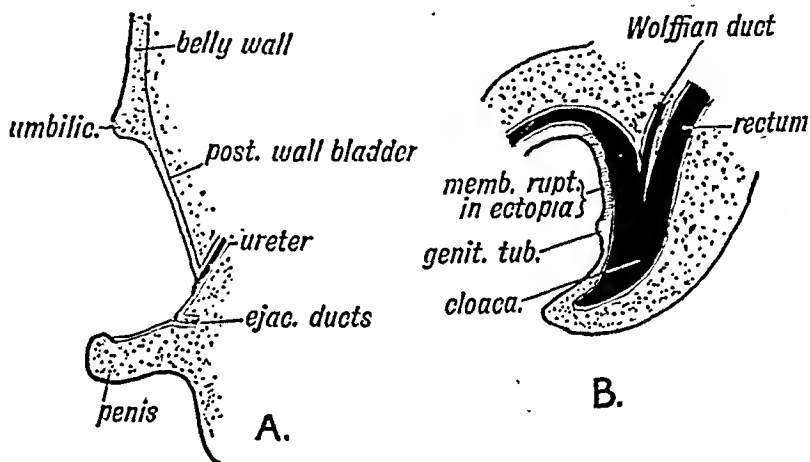


FIG. 487.

A. A section to show the condition of parts in *Ectopia Vesicae*.

B. Section of the Pelvis of an Embryo (5th week) to show how the condition is probably produced.

embedded in the subperitoneal tissue and flanked on each side by the umbilical artery. In the 7th month the apical part of the bladder is attached by a mesentery to the anterior wall of the abdomen; later the mesentery disappears (Broman).

Bladder at Birth.—At birth the bladder is elongated and fusiform in shape, with a small trigone. The capacity of the true pelvis is relatively less than in the adult; hence the greater part of the bladder is supra-pubic in position.

Ectopia vesicae.—This condition is shown diagrammatically in Fig. 487, A. The anterior wall of the bladder and roof of the urethra and the parts of the belly-wall in front of these are absent; the trigone, floor of the urethra and posterior wall of the bladder are flush and continuous with the belly-wall. The opposite halves of the symphysis pubis remain apart. Dr. Florian's researches have shown that the cloacal membrane,

which represents the original orifice of the cloaca, extends on to the body-stalk during the 4th week of development (see Fig. 45, p. 55). Normally, the part of the cloacal membrane which lies along that part of the allantois which becomes the bladder (Fig. 487, *B*), is obliterated by the ventral mesoderm on each side, which invades the membrane and thus forms the infraumbilical part of the abdominal wall as well as the genital eminence—in fact, all the tissues in the mid ventral line, between the urethral meatus and the umbilicus. If this process of fusion along the median line fails, then we have the condition seen in ectopia vesicae. If we accept the primitive streak—of which the cloacal membrane is the hindmost part—as the representative of the blastopore or primitive mouth, then ectopia vesicae reproduces an extremely remote ancestral condition [17]. In some cases the cleft lays open not only the bladder but also the mid-gut [18].

Musculature of the Bladder, Urethra and Rectum.—Seeing that the rectum, allantois and cloaca are continuous in the embryo one would expect that the musculature of the parts should show traces of this continuity. Prof. F. Wood-Jones found: (i) that the band of musculature which passes from the front of the rectum to be lost in the tissue behind the membranous urethra is a remnant of the recto-cloacal communication in the embryo (Fig. 479); (ii) that the circular muscular coat of the urethra is continuous above with the sphincter and circular coat of the bladder, and below it becomes continuous with the striated fibres (constrictor urethrae) surrounding the membranous urethra. The latter, however, are not developed from the musculature of the urogenital sinus, but from the sphincter cloacae (Fig. 486).

The prostate [19] is developed by outgrowths of the endoderm lining the upper part of the urogenital sinus and from the mesodermal tissue surrounding the sinus. It consists of glandular tissue and stroma.

(i) The *glandular tissue* is composed of tubular glands which open into the prostatic part of the urethra. They are developed in the 4th month, as a series of solid buds, about 60 in number, from the epithelium lining the upper part of the urogenital sinus (Fig. 488). The buds, which soon become tubular, arise from a right and left longitudinal furrow or fold of the wall of the sinus between which the Wolffian ducts open. The prostatic furrows reach upwards above the Wolffian openings, and that of the uterus masculinus, into the purely urinary part of the sinus and downwards into the part which serves as a common passage for the semen and urine. These segments of the sinus become the *upper and lower parts* of the prostatic urethra. The buds from the right and left furrows form two lateral masses or lobes. Besides the two lateral lobes there are three other outgrowths. One of these constitutes the 3rd

or intermediate lobe; its tubules arise from the dorsal or rectal wall of the urogenital sinus just above (proximal to) the openings of the ejaculatory (Wolffian) ducts. They grow towards the internal meatus and trigone of the bladder. A fourth group of glands—the posterior—also arises from the dorsal or rectal wall of the sinus, but from that part which lies below (distal to) the openings of the ejaculatory ducts. The posterior group of glands occupies the whole of the aspect of the prostate directed towards the rectum. Lastly, a fifth group arises from the anterior or pubic side of the sinus; this group serves to unite the lateral lobes on the pubic or anterior aspect of the urethra. This outgrowth makes up the anterior commissure of the prostate, which is formed only in man and in the great anthropoids. Not all the glandular outgrowths reach the surface of the prostate; many of those of the lateral lobes remain in the periurethral tissue. New tubules continue to be formed

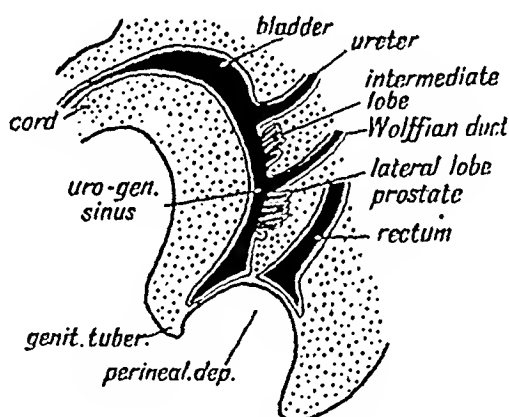


FIG. 486. A diagram to show the position at which the Prostatic Tubules arise.

throughout childhood and especially at puberty, when glandular alveoli are developed. The use of the prostatic secretion is unknown. The prostate seems to have been evolved out of the glands of the reptilian cloaca.

Skene's tubules, which open into the urethra of the female, represent prostatic tubules. A reference to Figs. 479, 480 will show that the female urethra corresponds to the upper prostatic urethra of the male and that Skene's tubules correspond to the upper prostatic tubules of the male.

(ii) *Stroma of the Prostate*.—While the glandular tubes arise in linear groups from the epithelium lining the urogenital sinus, the muscular and fibrous elements are derived from the mesodermal tissue of the genital cord in which the terminal parts of the Wolffian and Müllerian ducts are situated (Fig. 461) and from the circular musculature of the urogenital sinus. When the glandular elements grow out they become embedded in and carry before them the circular musculature of the

urogenital sinus which thus forms the muscular cortex or inner capsule of the prostate (Fig. 490). Probably the stroma of the genital cord also contributes to the musculature of the prostate. The musculature of the uterus, which is also developed from the genital cord, like that of the prostate, is liable to become the seat of fibromyomatous growths in the later years of adult life.

As regards the nature of the prostate [20]: (i) It is purely genital, and develops only in the rutting season in such mammals as manifest a seasonal sexual life. Its development in the female is arrested at a very early stage—due to the inhibitory action of the female (oestrogenic)

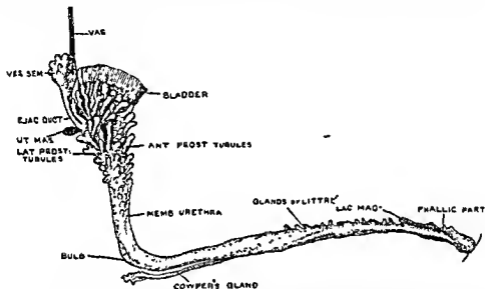


FIG. 489 The Prostate and Urethra towards the end of the 4th month (After Broman and Eratt). The phallic part of the urethra ends posteriorly at the lacuna magna. It is developed in the glans penis. The uterus masculinus (ut mas) is indicated diagrammatically to show its relationship to the common ejaculatory duct.

hormone. Certain epithelial elements of the prostate, particularly those which line the uterus masculinus and the neighbouring tubules of the intermediate lobe, are in a hyperplastic state at birth, due to the action of the female (oestrogenic) hormone derived from the maternal circulation (Zuckerman). The rapid proliferation at puberty is due to the action of the male (androgenic) hormone. (ii) It remains comparatively undeveloped until puberty. At the age of 7 it weighs only 30 grains; after sexual life is established it weighs about 300 grains. (iii) The healthy prostate atrophies if castration is performed, but this operation has no effect on glands which have become pathologically hypertrophied [21]. In one man out of three over 55 years of age the prostate hypertrophies, both the glandular and fibro-muscular elements participating. Hypertrophy of the median part causes a valvular elevation behind the vesical opening of the urethra.

Glands of Cowper and Bartholin are produced as solid buds from the endodermal lining of the penile extension of the urogenital sinus (Fig. 489). Hence in the female the ducts of Bartholin's glands open in the vulval cleft just outside the hymen at each side of the vagina, for the hymen marks the junction of the Müllerian ducts with the urogenital sinus. In the male the ducts of Cowper's glands open in the bulbous part of the urethra (Fig. 489). The function is unknown, but it is certainly sexual in nature, for these glands atrophy after castration. The numerous *glands of Littré*, like Cowper's and Bartholin's glands, are produced by

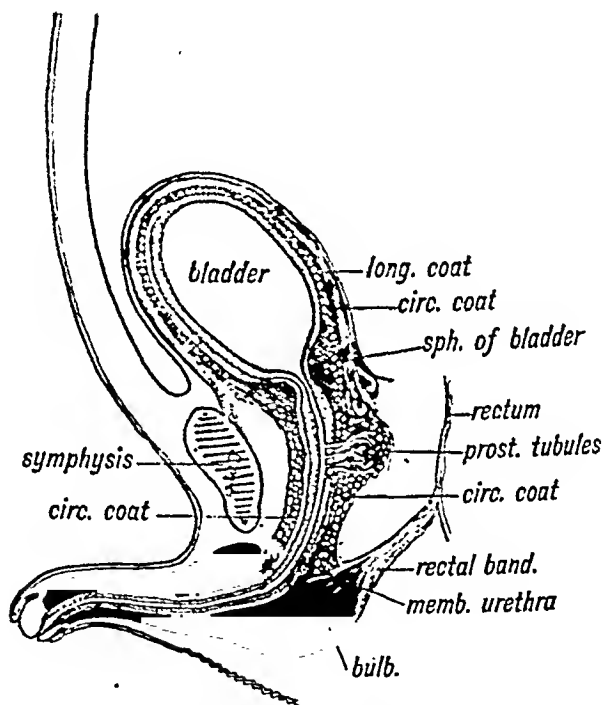


FIG. 490. Diagrammatic section of the Bladder and Urethra of a 6th-month Foetus to show (1) the development of the Prostate, (2) the relationship of the Prostatic Musculature to that of the Urethra and Bladder. (Wood-Jones.)

tubular outgrowths during the 4th month (Fig. 489). In the male the glands of Littré are produced most numerous along the dorsal aspect of the urethra.

Round the anus, and especially in the furrow between the labium minus and majus, groups of large peculiar sebaceous glands are produced in the 4th and 5th months, corresponding to the *anal* and *preputial* glands of mammals. Occasionally two groups of sebaceous glands occur on the prepuce of the male, especially if hypospadias be present (Shillitoe). Glands round the corona of the glans penis (*Tyson's glands*) are only very exceptionally present.

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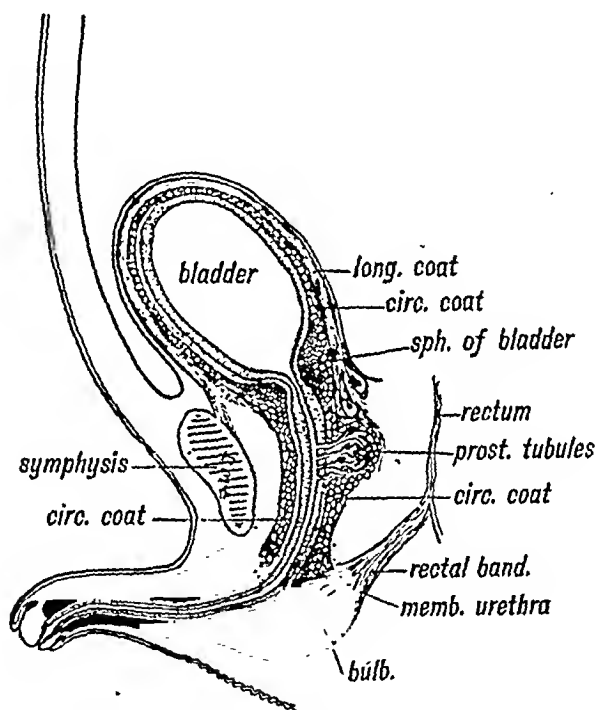


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- [1] Wood-Jones, F., *Jour. Anat.*, 1914, 48, 73; 1915, 49, 393; 1916, 50, 1, 189.
- [2] For development of cloaca, see Shikunami, J., *Contrib. Emb.*, 1926, 17, 49; Pohlman, A. G., *Amer. Jour. Anat.*, 1911, 12, 1; Frazer, J. E., *Jour. Anat.*, 1935, 69, 455; Politzer, G., *Zeitsch. Anat. Entwickl.*, 1934, 102, 690; Tench, E. M., *Amer. Jour. Anat.*, 1936, 59, 333 (development of anal canal).
- [3] As to the manner in which the rectum becomes separated from the urogenital sinus we have to interpret developmental happenings in the light of comparative anatomy. The developmental appearances can be interpreted as a migration of the anus to the perineum, and from an evolutionary point of view the migratory interpretation is the more probable.
- [4] For the sake of uniformity of nomenclature it would be well to name the marginal folds of the ectodermal cloaca "outer genital" and those of the urogenital orifice the "inner genital."
- [5] For development of rectum and anus: Johnson, F. P., *Amer. Jour. Anat.*, 1914, 16, 1; Wakeley, C. P. G., *Jour. Anat.*, 1923, 57, 216; Harris, H. A., *Proc. Roy. Soc. Med.*, 1929, 22, 43 (Sect. of Proctology); see also references to Politzer and to Tench in note [2].
- [6] For development of the external genital organs, see Spaulding, M. H., *Contrib. Emb.*, 1921, 13, 69; Wilson, K. M., *ibid.*, 1926, 17, 25; Popper, R., *Zeitsch. Anat. Entwickl.*, 1937, 107, 378; Ashley-Montagu, M. F., *Anat. Rec.*, 1937, 69, 389 (in primates).
- [7] See note [4].
- [8] For development of the urethra, see Johnson, F. P., *Jour. Urology*, 1920, 4, 447. In the text I have described the floor of the penile urethra as formed not by a union of the inner genital folds but as a forward growth of the urogenital orifice. In the female this orifice forms the vulval cleft; in the male it becomes the primitive opening of the urethra. If the floor of the male urethra were formed by the union of the inner genital folds one would expect to find a median raphe.
- [9] For development of prepuce, see Frazer, J. E., *Manual of Embryology*, 1940; Wood-Jones, F., *Brit. Med. Jour.*, 1910, 1, 137; Hunter, R. H., *Jour. Anat.*, 1936, 70, 68; Deibert, G. A., *Anat. Rec.*, 1933, 57, 387.
- [10] For malformations of the urinary tract, see Thompson, R., *Jour. Anat.*, 1919, 53, 32; *Proc. Roy. Soc. Med.*, 1931, 24, 47 (Sect. of Urology).
- [11] Goldschmidt, R., *Die Sexuellen Zwischenstufen*, Berlin, 1931; Allen, E., *Anat. Rec.*, 1928, 39, 315; Humphrey, R. R., *ibid.*, 1931, 51, 135; Parkes, A. S., *Internal Secretions of the Ovary*, London, 1929.
- [12] See note [8].
- [13] The epithelial part of the urethra is formed by the union of the inner genital folds.
- [14] Otis, W. J., *Anat. Hefte*, 1905, 30, 199.
- [15] For development of the bladder, see Frazer, J. E., in note [2]; Czarski, C., *Anat. Anz.*, 1937, 84, 241 (separation of ureters); Silvestri, U., *Archiv. Ital. Anat. Emb.*, 1933, 32, 1 (musculature); Graening, W., *Zeitsch. Anat. Entwickl.*, 1937, 106, 226 (comparative anatomy of musculature); Harris, H. A., *Jour. Anat.*, 1926, 60, 328.
- [16] Hammond and Others, *Anat. Rec.*, 1941, 80, 271; Begg, R. C., *Jour. Anat.*, 1930, 64, 170; Doran, A., *Proc. Roy. Soc. Med.*, 1908, 2, 197 (surg. sect.).

[17] For accounts of ectopiae vesicae, see Wood-Jones, F., *Jour. Anat.*, 1912, 46, 193; Anders, H. E., *Virchow's Archiv.*, 1921, 229, 531; Brickel, A. C. J., *Anat. Rec.*, 1927, 34, 1; Keith, Sir A., *Brit. Med. Jour.*, 1908, 2, 1,736 *et seq.*; Paterson and Emrys-Roberts, *Jour. Anat.*, 1906, 40, 332.

[18] See references in note [17], particularly those under the names of Wood-Jones, Anders, and Keith.

[19] For development of prostate, see Lowsley, O. S., *Amer. Jour. Surg.*, 1930, 8, 526; Hirsch, E. W., *Jour. Urology*, 1931, 25, 669; Evatt, E. J., *Jour. Anat.*, 1909, 43, 314; 1911, 45, 122; Wagenen, G. van, *Anat. Rec.*, 1936, 66, 411 (prostate of monkeys).

[20] For effects of male and female hormone substances on the various elements of the prostate: see summaries published by Prof. S. Zuckerman in *Proc. Roy. Soc. Med.*, 1936, 29, 81 (Sect. Urol.), and in *Biol. Revs.*, 1940, 15, 231; see also his contributions made alone, or in partnership with others, in the *Jour. Anat.*, 1935, 69; 1936, 70; 1938, 72; 1939, 73; *Jour. Path. Bact.*, 1938, 46, 7 (enlarged prostate of dogs). For experiments on the genital system of mice: Burrows, H., *Proc. Roy. Soc.*, 1935, 131 (B), 485; *Nature*, 1936, 138, 164; *ibid.*, 1939, 143, 858; Deansley, Ruth, *Proc. Roy. Soc.*, 1938, 126 (B), 122; Brambell and Davis, *Jour. Anat.*, 1941, 75, 64; Price, Dorothy, *Amer. Jour. Anat.*, 1936, 60, 39 (in rats); Moore, R. A., *Anat. Rec.*, 1936, 66, 1 (human prostate at birth); Swyer, G. I. M., *Jour. Anat.*, 1944, 78, 130 (changes in human prostate after birth); Ivanov and Kassavina, *Nature*, 1946, 158, 624 (action of prostatic secretion on spermatozoa).

[21] Riches and Muir, *Brit. Jour. Surg.*, 1933, 20, 366; Wallace, Sir C., *Trans. Path. Soc. Lond.*, 1905, 56, 80.

CHAPTER XXVII

UROGENITAL SYSTEM (continued)

TESTIS AND ADRENAL BODY

This is the last of three chapters devoted to a consideration of the origin of the urogenital system of the human body. In the first of these chapters we dealt with the rise of the Wolffian body and the duct system connected with that body. In the second we passed in review the development of the uterus and vagina, the separation of the rectum from the urogenital system and the formation of the external organs of generation. We are now to note the rise of the testis and of its ducts. We shall also consider the adrenal body, which, like the pituitary, is closely linked to the sexual system.

Attachment of the Testis.—The origin [1] of the testis on the inner or

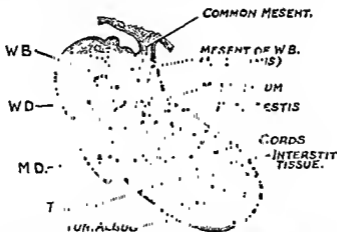


FIG. 491 Section to show the Attachments of Testis and Wolffian Body to Dorsal Wall of Abdomen in 7th week. W.B., Wolffian body; W.D., Wolffian duct; M.D., Mullerian duct.

mesial side of the Wolffian ridge and its attachment to the dorsal wall of the coelom by a mesentery common to it and the Wolffian body have been already described (see Figs. 4, 26, 491). Its position at the beginning of the 3rd month is shown in Fig. 492. Although in the 6th week the genital ridge extended from the 6th to the 12th thoracic segment, the testicle, developed from the hinder part of the ridge, is now situated in the iliac fossa. The mesorchium (Fig. 491), a fold of peritoneum, binds its attached border to the iliac fossa. At its outer side lies the genital part of the Wolffian body which forms the epididymis. It also

is suspended by a mesentery—the Wolffian mesentery. The two mesenteries have a common base—the common urogenital mesentery (Fig. 491). The upper part of the urogenital mesentery forms the diaphragmatic fold, with which the peritoneal fold containing the spermatic artery becomes joined; to the combined fold is given the name of *plica vascularis* (Fig. 492). This in the female becomes the ovario-pelvic ligament (Fig. 5). A fold of peritoneum, the inguinal fold or *plica gubernatrix*, continues the common urogenital mesentery to the groin (Fig. 492). The gubernaculum testis is developed in the *plica gubernatrix*; in the corresponding fold in the female the round

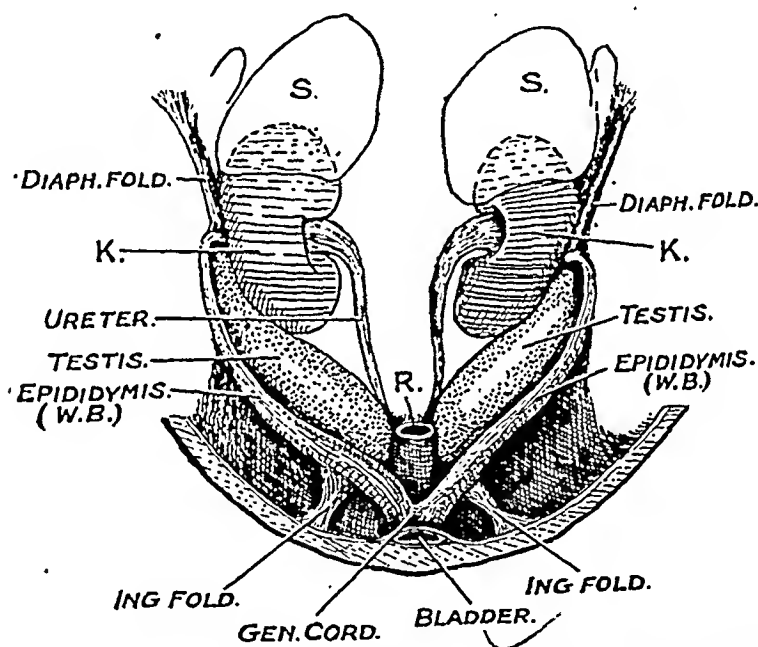


FIG. 492. The Position and Attachments of the Testes early in the 3rd month of development. K., kidney; S., suprarenal; W.B., Wolffian body; *ing. fold*, inguinal fold; R., rectum.

ligament of the uterus appears (see p. 518). The vas deferens (Wolffian duct) turns into the pelvis from the lower end of the epididymis (Wolffian body), and within the pelvis lies in the genital cord (Fig. 492). A remnant of the Müllerian duct lies along the inner and ventral aspect of the epididymis (Fig. 491).

Seminiferous Tubules.—The arteries for the genital glands represent the lowest of the vessels which supplied the Wolffian body and arise from the aorta at the level of the 12th dorsal vertebra; their nerve supply comes from the 10th dorsal segment of the spinal cord. The testis is therefore developed in the genital ridge between the 10th and 12th dorsal segments. The early development of the testis is similar to that of the ovary. Up to the 7th week, when the embryo measures 15 mm. in

length, it is impossible to tell testicle from ovary; both of them at this time show a covering of germinal epithelium and deep central masses or columns of epithelioid cells derived from the covering layer of germinal epithelium. In the central masses are the large primitive germinal cells or gonocytes. At the end of the 7th week two changes lead to the differentiation of a testis from an ovary: (i) a tunica albuginea begins to form under the superficial epithelium; (ii) the central masses proliferate and form radiating cords which branch as they spread from hilum to periphery. The cords become transformed into the seminiferous tubules, which are at first solid; they anastomose at their peripheral ends. Some of the epithelioid cells are not included in the tubules and remain to form *interstitial cells* [2]. The germinal cells (gonocytes) are included in the epithelial cords. The tubules become separated into groups or compartments in the 6th month and about the same time lumina are formed in them. The formation of spermatozoa has been already described (p. 12). The visceral layer of the tunica vaginalis on the testicle represents the covering of flattened epithelium which remains after the ingrowth of the germinal epithelium. The vasa efferentia and coni vasculosi are formed from the *genital* Wolffian tubules; the rete testis and vasa recta from the junctional cords (p. 509). Towards the end of the 3rd month the rete effects a communication with the tubuli seminiferi on the one hand and with the vasa efferentia on the other. The epididymis is the elongated and coiled segment of the Wolffian duct (Fig. 453). The Wolffian elements are produced within the Wolffian ridge (Fig. 459).

The Pubic Apron.—When describing the inguinal fold (p. 518) I drew attention to the fact that the fibroblasts within it were in continuity with the mesodermal tissues of the inguinal and prepubic regions. The prepubic tissue, which may be named the "pubic apron," is illustrated in Figs. 493, *A*, *B*, *C*, taken from Dr. Moszkowicz's monograph [3]. About the middle of the 3rd month (foetal) this special area of subcutaneous tissue (Fig. 493, *A*) lies above the root of the penis and in front of the symphysis, extending to the groin on each side, where it receives the inguinal ligaments, which serve it as apron strings. Three weeks later, at the end of the 3rd month (*B*), several changes have taken place. The tissue of the apron now appears swollen, its fibro-cellular elements being in a state of active proliferation; in brief, the apron has come under the influence of the sex hormones, both oestrogenic and androgenic. The penis, instead of drooping as in *A*, is now raised and applied to the ventral (front) aspect of the symphysis. The tissue of the apron, in place of being confined to the region of the symphysis, has become extended toward the anus, thus providing tissues for the forma-

tion of the scrotum (see Fig. 483, *A*). In a female foetus of the same age (*C*), the pubic apron, although it has increased in size, still retains the earlier relationships. The tissue which goes to form the scrotum of the male remains quiescent in the labia majora of the female. Thus there are two mesodermal invasions of the human perineum; there is the early invasion that establishes its central part in the later part of the 2nd month; there is the later invasion that is peculiar to the male, the invading scrotal tissues being derived from the pubic apron.

The pubic apron is a structure of ancient origin, having been evolved in connection with the Wolffian body and sex glands. In lower mammals the pubic apron provides the material in which mammae and marsupial

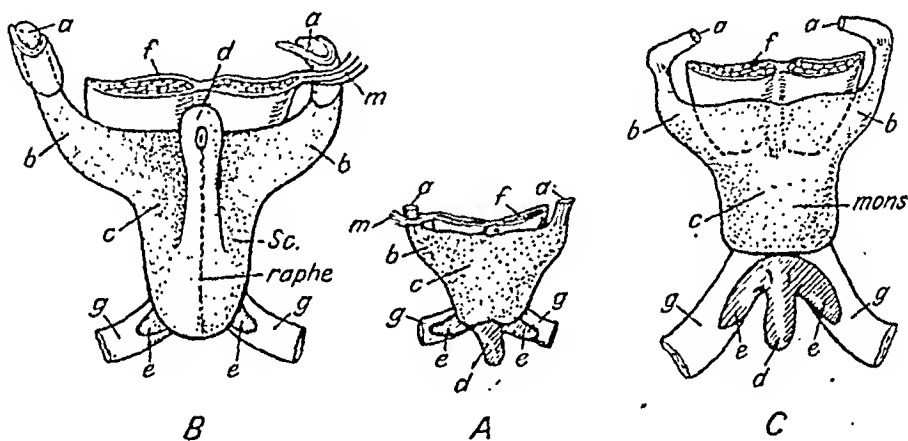


FIG. 493.

A. The "Pubic Apron" of a Male Foetus of 11 weeks.

B. The same at the end of the 3rd month.

C. The same in a Female Foetus of 3 months (all three figures modified from Moszkowicz).

a, inguinal cord in abdomen; *b*, the same in the groin; *c*, prepubic subcutaneous tissue constituting the "pubic apron"; *d*, penis or clitoris; *e*, crus penis; *f*, rectus abdominis; *g*, pubic ramus; *m*, muscles of the inguinal region; *Sc.*, scrotum. The raphe is indicated.

pouch are developed. In the Primates its tissues are swollen at birth (oestrin effect) and also swell and redden during periods of heat [4].

The Gubernaculum Testis [5].—Mention has been made of the early connection established between the inguinal fold within the abdomen and the pubic apron in the groin. When the musculature of the abdominal wall becomes differentiated late in the 2nd month, the inguinal ligament or strand can be seen to be made up of three segments—intra-abdominal, interstitial and extra-abdominal. The interstitial segment receives contributions from the musculature of the abdominal wall. Early in the 4th month the subperitoneal non-striated muscular tissue in the plica gubernatrix and in the mesorchium takes on a rapid and organized growth (Fig. 494). At the same time the tissues of the

abdominal wall also share in this growth movement, undergoing a localized evagination towards the scrotum. They are carried down by the growth of the gubernacular bud, which works its way to the scrotum. The gubernaculum grows downwards as a solid mass until it reaches the subcutaneous tissue which by this time completely fills the scrotum. Its attachment to the scrotum is slight and easily broken (Fig. 494). The gubernaculum, as it grows through the abdominal wall in the track of the inguinal strand, carries with it: (i) a process of peritoneum (the processus vaginalis); (ii) the transversalis fascia (the infundibuliform fascia); (iii) the internal oblique and transversalis muscles to form the cremaster; (iv) the spermatic fascia from the external oblique; (v) the

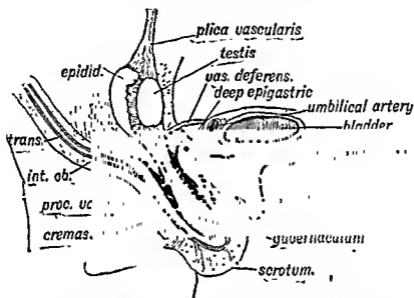


FIG 494. Showing the Position of the Testis in the 6th month, and the Formation of the Gubernaculum Testis

deep layer (Scarpa's) of the superficial fascia of the groin. All these layers are added to the primitive coverings of the scrotum, which until then was made up simply of skin and the peculiar subcutaneous tissue or superficial fascia just described (p. 553) (Fig. 494).

It will thus be seen that the gubernaculum testis is a fibro-muscular mass with an actively growing cellular cap, which, starting from the muscular stratum in the mesorchium and plica gubernatrix in the iliac fossa, invades the abdominal wall, every layer of which participates in the growth movement, and is carried with the gubernacular bud towards the scrotum. The gubernaculum, sharing the organizing properties of the sub-peritoneal tissues, behaves like an invading army. The growth process stimulated by the sex growth hormones [6] loosens the tissues into which it advances, while the pressure within the abdomen generated

tion of the scrotum (see Fig. 483, *A*). In a female foetus of the same age (*C*), the pubic apron, although it has increased in size, still retains the earlier relationships. The tissue which goes to form the scrotum of the male remains quiescent in the labia majora of the female. Thus there are two mesodermal invasions of the human perineum; there is the early invasion that establishes its central part in the later part of the 2nd month; there is the later invasion that is peculiar to the male, the invading scrotal tissues being derived from the pubic apron.

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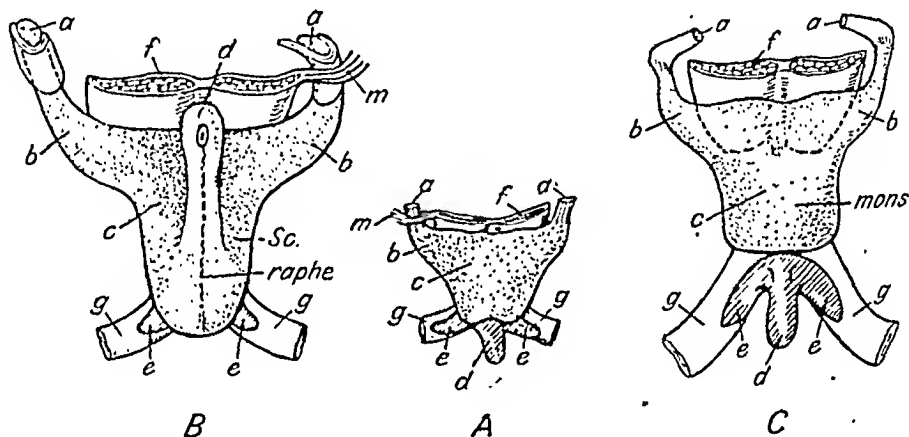


FIG. 493.

A. The "Pubic Apron" of a Male Foetus of 11 weeks.

B. The same at the end of the 3rd month.

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a, inguinal cord in abdomen; *b*, the same in the groin; *c*, prepubic subcutaneous tissue constituting the "pubic apron"; *d*, penis or clitoris; *e*, crus penis; *f*, rectus abdominis; *g*, pubic ramus; *m*, muscles of the inguinal region; *Sc.*, scrotum. The raphe is indicated.

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Descent of the testicle may be arrested at any stage: often in the inguinal canal, more frequently at the external abdominal ring. Arrest of descent is commonly regarded as a symptom of arrest of testicular development. John Hunter regarded a congenital arrest of the descent of the testicle as due to an imperfection in its development [8]; we, in the light of present knowledge, attribute it to a defect in the production or interaction of sex hormones. On the other hand, the testicle may assume an *ectopic* position. The gubernaculum as it makes its way towards the scrotum may take an eccentric course and bring the testicle to rest in the groin, at the root of the penis, or over the pubis.

Why do the testes of most mammals leave the abdomen? There is

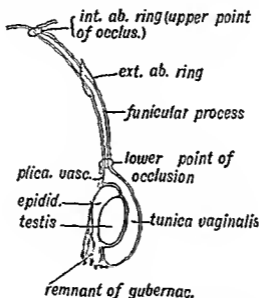


FIG. 496. A Diagram of the Processus Vaginalis

still much debate. Prof. Crew and others have brought forward evidence to prove that the temperature within the abdomen is too high for the ripening of spermatozoa [9]. The high temperature of birds does not affect intra-abdominal spermatogenesis; Badenoch found that in men the mean temperature within the scrotum was only 2.2°C . lower than within the abdomen. For my part I think the evidence favours the theory that testicles seek the scrotum to escape the sudden and high pressures to which the abdominal viscera are subjected during strenuous movements. Mammals which retain the testes within the abdomen are stiff-bodied. Testicular descent is correlated with the evolution of the diaphragm and exclusion of the lungs from the abdominal cavity [10]. From some cause at present not understood, a testicle atrophies when subjected to this pressure [11]. It also atrophies if subjected to a constant dosage of oestrone.

by its muscular wall adds a thrusting force. The peritoneum of the iliac fossa to which the testis is attached also participates in the growing, migratory process. Thus we may regard the descent of the testicle as a form of developmental hernia.

We have seen how a rapid growth and extension of the lumbar part of the vertebral column during the 3rd month carries the kidneys away from the pelvis, while the testes (and also the ovaries) are left level with the iliac crest (Fig. 458). Thus, as Lockwood observed in 1883 and Wyndham in 1943, the testes lie in the iliac fossa close to the groin from the 3rd to the 7th month of foetal life. The 7th month is spent in their transit of the abdominal wall. In the 8th month they leave the inguinal canal and pass the external ring. After birth the fundus of the scrotum

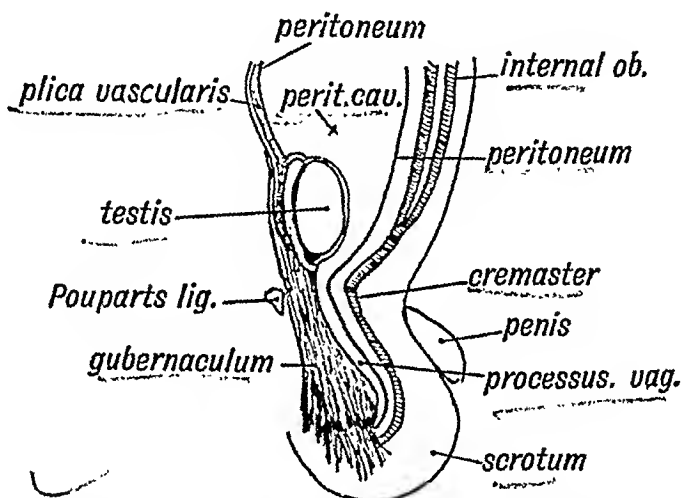


FIG. 495. The manner in which the Structures in the Wall of the Abdomen are carried outwards so as to form the Inguinal Canal and Coverings of the Testis.

is reached. A remnant of the gubernaculum can always be found in the adult, within the mesorchium (Fig. 496).

Processus Vaginalis.—The processus vaginalis becomes occluded by adhesion or zygosia (p. 407) at two points at or soon after birth, but in a considerable proportion of individuals the process of closure is delayed (Fig. 496). The upper point of occlusion takes place at the internal abdominal ring; the lower a short distance above the testicle. The part of the processus vaginalis between the points of occlusion is known as the *funicular process*; the part surrounding the testicle becomes the tunica vaginalis. In quite 30% of children the occlusion takes place at the internal abdominal ring some considerable time after birth or it fails altogether [7]. Occlusion may fail at the upper point, at the lower point, or at both. Or it may close at both points, but the funicular process, instead of disappearing, may remain open and form a cyst.

such cases, then, the gubernaculum has not extended to the upper part of the inguinal fold.

Inter-Sex and Imperfect Sex [12].—Embryos of the 7th week possess rudiments of both sexes; the male embryo, so determined by its chromosome constitution, possesses Müllerian ducts; the female, similarly determined, is provided with Wolffian ducts. Some factor comes into operation in the 7th week which determines the direction of sexual development. There is evidence that this factor may be of the nature of a hormone (Lillie). Certain intersexes are produced in the following way. In cases where twins have been conceived, a placental intercommunication may be effected between the two foetal circulations. If both twins are of the same sex no harm results, but if they are of opposite sexes then the female undergoes a sexual change. Male characters are dominant; they appear (in the gonadal glands of males) at least a week earlier than do those of females; male embryos are first off the mark towards sex differentiation. Where the circulations are in communication something (androgenic hormone) is carried by the blood from the male gland to the gonads of the female twin; that something alters the sexual development of the twin so that the ovaries become imperfect testes; the differentiation of the Müllerian ducts is arrested, the external genitals assume an intersexual form. Such twins, females by chromosomal constitution, imperfect males by hormonal influence, are known as *free-martins* [13]. Imperfect males may result from a defect in chromosomal constitution; imperfect females—where the gonad is truly an ovary, but the external genitals assume the imperfect male form—are very rare. Secondary sexual characters are determined mainly by testicular (interstitial) and ovarian hormones; but evidence is not lacking to show that they are also influenced by the pituitary gland and cortex of the suprarenal (see p. 166).

Hermaphrodites [14].—An hermaphrodite—a human individual in which both testis and ovary are present with power of self-fertilization—has never been seen. In 1909 Prof. Wm. Bulloch found only five cases on record in which, within the same genital gland, there were present representations of imperfect testicular and ovarian tissues (ovo-testis); functional spermatozoa and ova were not present. In recent years many more cases have been recorded. The term, however, is usually (but wrongly) applied to individuals in whom the genital glands are imperfectly developed. As we have just seen, most of these are imperfect males. Testes and ovaries seem to exercise an opposite effect on the development of sexual structures. Hence, if the gonads of an individual are imperfectly differentiated development of its genital parts is uncontrolled; such an individual assumes a sexual form which may best

Mesorchium.—At first, the testis and epididymis are suspended within the abdomen by the common urogenital mesentery (Fig. 491). In the course of the descent of the testis this becomes shortened by the development of the gubernaculum, the testis and epididymis becoming thus firmly bound by their posterior borders to the tunica vaginalis. The digital fossa, situated between the mesorchium and mesentery of the Wolffian body, represents the recess which separated the genital from the Wolffian ridge of the embryo. The mesorchium—the true mesentery

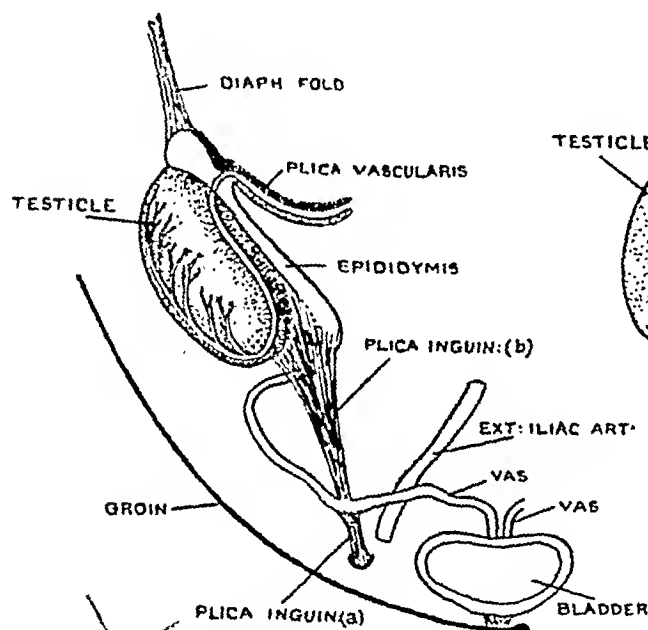


FIG. 497.

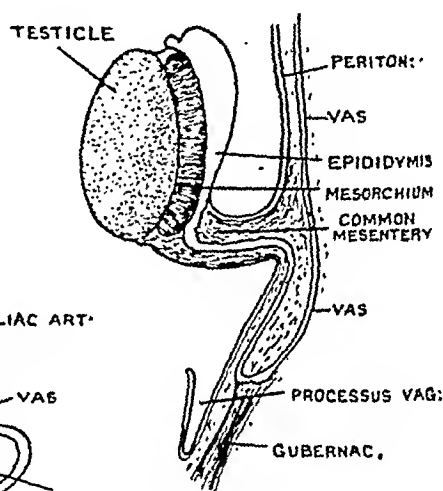


FIG. 498.

FIG. 497. To show the Diaphragmatic Fold (upper part of the common genital mesentery), Vascular Fold, and the two parts of the Inguinal Fold in a Foetal Pig. (Eben. C. Hill.)

FIG. 498. Elongated Common Mesentery of a Human Testicle arrested in the course of its descent.

of the testicle—may assume the form of an elongated fold, attaching the testicle to the epididymis.

A not unusual anomaly of the testicle is represented in Fig. 498. It will be observed that the common mesentery, in place of becoming shortened, and thus fixing the testicle and epididymis widely to the peritoneum, becomes narrow and elongated. Such testicles are usually arrested in their descent, and are apt to twist and become strangulated. It will also be observed that a gubernaculum is present, but it has seized and drawn downwards only a loop of the vas deferens. The explanation is shown in Fig. 497. The inguinal fold is made up of two parts, *a lower*, ending on the vas deferens and corresponding to the round ligament of the female; *an upper*, which continues the fold to the epididymis and testicle, and which corresponds to the round ligament of the ovary. In

of the 7th week the cortex is in place, with the neural element assembled on its dorso-medial aspect (Fig. 500). The suprarenals are developed within the anterior ends of the Wolffian bodies, just behind the pleuro-peritoneal passages. The *medulla* arises from groups of sympathetic cells—probably from the primitive cell basis of the semilunar ganglion, which is developed by the side of the aorta, close to the pleuro-peritoneal opening. The nerve fibres which end on the ganglionic cells and control their secretion (adrenalin) arise from the visceral cell column of the spinal cord and therefore belong to the preganglionic system. They have a segmental termination in the medulla (J. Z. Young). The medullary cells begin to migrate into the cortex in the 8th week; the process of invasion is continued through the greater part of foetal life. Prof. Lucas Keene and Dr. E. Hewer found that the chromaffin reaction on the cells of the medulla appeared in the 22nd week, while adrenalin was detectable in the 12th week [17]. By the beginning of the 4th month the medulla is arranged as reticulating columns set on the walls of branching venous sinuses.

The cortical cells range themselves in rows between radiating blood sinuses. At birth the innermost zone—that which is in contact with the medulla—has peculiar characters. This zone of *foetal cortex* undergoes a rapid degeneration, commencing before but becoming markedly accelerated just after birth [15]. It is possible that the production of foetal cortex is due to the action of oestrogen—which also brings about a ripening of follicles in the ovaries and growth of the cervix of the uterus in female children. As the kidneys ascend in the 3rd month they come in contact with the suprarenal bodies. The suprarenal is at first larger than the kidney (Fig. 458, p. 514), even at birth they are nearly equal in size. The nerves and arteries enter the bodies on their renal surface; the veins emerge on their anterior (ventral) surface.

Until the 3rd month of development the suprarenal bodies are in contact with the upper pole of the testis or ovary. As the genital glands descend, the diaphragmatic fold is drawn from the suprarenal region and frequently carries with it buds of suprarenal tissue both cortical and medullary. It can, therefore, be readily understood how isolated parts of the suprarenal body (accessory suprarenals) occur in the broad ligament or in the spermatic cord above the testicle. Such accessory bodies are probably derived from the cortical element which is developed within the Wolffian ridge and body. With the descent of the ovary and testicle, which bring with them the Wolffian body, adjacent accessory suprarenals, if such be present, are also brought down, and may occasionally give rise to peculiar tumours. Certain tumours which occur in the substance of the kidney and known as *hypernephromata* were at one time

be described as neutral. There is evidence to support the opinion that the embryonic genital gland is composite: the testicle develops within the medullary or central part of the gland; the ovary from its cortical or more superficial parts. The medullary field appears to have a power to override the chromosome constitution of the female, while the cortical field exercises a similar power over the male chromosomes. Also, it must be kept in mind that male and female sex hormones are produced in both sexes; it is the balance of these hormones which exercises the determining influence (Zuckerman).

Development of the Suprarenal Bodies [15].—The suprarenal or adrenal bodies arise by the association of two distinct embryological elements—*cortical* and *medullary*. In Fig. 500 is given a diagrammatic section to show the stage reached in the 7th week of development, the

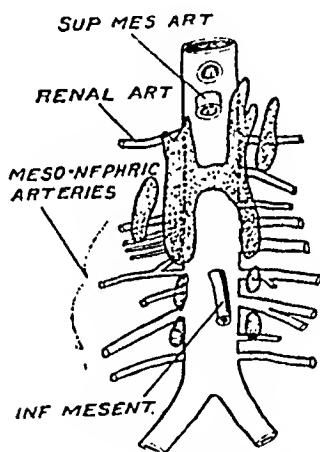


FIG. 499.

FIG. 499. Showing the distribution of the Aortic Chromaffin Bodies in the early Human Foetus. (After Zuckerkandl.)

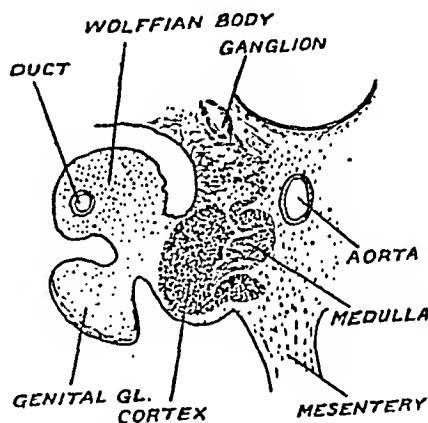


FIG. 500.

FIG. 500. Section across the Suprarenal, Genital and Wolffian Bodies in an Embryo in the 7th week, 15 mm. long. (After Zuckerkandl.)

cortical element then being large and projecting at the root of the mesentery and in contact with the genital and Wolffian bodies, while the medullary element consists of neuroblasts derived from the blastema of the sympathetic system. These neuroblasts give rise to ganglionic nerve cells which have a secretory function. The *cortical element* is associated with the genital system; its secretion regulates the development of certain sexual structures and functions [16]. Like the epithelioid cells of the genital glands, the cortex arises by an invagination of coelomic epithelium, the suprarenal ingrowth occurring on each side of the root of the mesentery early in the 6th week. Two broods of cells arise from the coelomic epithelium. The first provides the basis of the inner or foetal cortex; the later, the outer or permanent cortex. By the end

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[5] For descent of testicle, see Hunter, John, *Collected Works*, 1837, vol. 4, 1; Lockwood, C. B., *Jour. Anat.*, 1887, 21, 635; 1888, 22, 38 *et seq.*; Hunter, R. H., *Brit. Jour. Surg.*, 1927, 14, 125; *Ulster Med. Jour.*, 1933, October; Broek, Prof. van der, *Morph. Jahrb.*, 1929 (Maurer Festsch., p. 1); Kirk, John, *Jour. Anat.*, 1936, 71, 146; Wyndham, N. R., *ibid.*, 1943, 77, 179; Curl and Tromly, *ibid.*, 1944, 78, 148.

[6] For influence of sex hormones in bringing about descent of testicle: Burrows, Harold, *Brit. Jour. Surg.*, 1934, 21, 507; *ibid.*, 1936, 23, 658; *Jour. Path. Bact.*, 1935, 41, 218; 1937, 45, 311; Gardner, W. U., *Amer. Jour. Anat.*, 1936, 59, 459; Hamilton, J. B., *Anat. Rec.*, 1938, 70, 533; Wells, L. H., *Jour. Anat.*, 1935, 69, 508; *Anat. Rec.*, 1942, 82, 565; Kiesselbach, A., *Zeitsch. Anat. Entwickl.*, 1934, 103, 408; Bolliger, A., *Nature*, 1942, 150, 688. See also references given in note [4].

[7] Mitchell, G. A. G., *Jour. Anat.*, 1939, 73, 658.

[8] There is evidence that a testicle may be fully developed and yet fail to descend, see Cooper, Eugenia, *Jour. Anat.*, 1930, 64, 5; Kennedy, W. P., *ibid.*, 1927, 61, 353; Eisenstaedt, J. S., *Jour. Amer. Med. Ass.*, 1927, 89, 1389.

[9] Crew, F. A. E., *Jour. Anat.*, 1922, 56, 98; Moore, C. R., *Endocrinology*, 1924, 8, 493; *Anat. Rec.*, 1931, 48, 105; Bedenoch, A. W., *Brit. Med. Jour.*, 1945, 2, 601; Adell and Salisbury, *Anat. Rec.*, 1941, 80, 145; Wilhams and Cunningham, *Yale Jour. Biol. Med.*, 1940, 12, 309.

[10] Woodland, W., *Proc. Zool. Soc. Lond.*, 1903, 1, 319.

[11] Cooper, E., see note [8].

[12] For imperfect differentiation of sex: Needham, J., *Biochemistry and Morphogenesis*, 1942, p. 310; Zuckerman and Groome, *Jour. Anat.*, 1940, 74, 171; Burns, R. K., *Contrib. Emb.*, 1942 *et seq.*; Humphrey, R. R., *Amer. Jour. Anat.*, 1941, 69, 19; Crew, F. A. E., *Sex Determination*, 1933; Dantchakoff, V., *Bull. Biol.*, 1937, 71, 269 (changed sex of guinea-pigs by testosterone); Harlant, M., *Archiv. Biol.*, 1933, 44, 347 (influence of interstitial tissue of testis).

[13] For literature on free-martins, see Hunter, John, *Collected Works*, 1837, vol. 4, 34; Lilhe, F. R., *Jour. Exper. Zool.*, 1917, 23, 371; Crew, F. A. E., *Quart. Rev. Biol.*, 1927, 2, 249; Goldschmidt, R., *Die Sexuellen Zwischenstufen*, 1931; *Physiological Genetics*, 1938; Roberts and Greenwood, *Jour. Anat.*, 1929, 63, 87.

[14] Bulloch, W., *Treasury of Human Inheritance*, 1930, Pt. 3; Jordan, H. E., *Amer. Jour. Anat.*, 1922, 31, 27; Baker, J. R., *Jour. Anat.*, 1926, 60, 374; Girgis, A., *ibid.*, 1923, 57, 251.

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[16] Adrenal cortex and sex: Broster and Vines, *The Adrenal Cortex*, 1933; Broster, L. R., *Brit. Jour. Surg.*, 1939, 26, 925; Hodler, D., *Archiv. d'Anat. Hist.*

supposed to arise from suprarenal rests. This is now known not to be the case; hypernephromata arise from nephrogenic rests [18].

Chromaffin Cells.—The medullary part of the suprarenals belongs to a segmental series of organs. In fishes such as the shark and lamprey, a group of cells (a paraganglion) is thrown off from each ganglion of the sympathetic chain and comes into close contact with the tributaries of the cardinal veins [19]. These cells stain brown with salts of chromium—hence their name; some of these cells remain within the sympathetic ganglia. Similar minute chromaffin bodies (paraganglia) are also developed in or near all the ganglia of the vertebral chain of the human foetus (see p. 356). Other collections of chromaffin cells arise at the sites of the prevertebral ganglia and plexus—such as the superior and inferior mesenteric plexuses. The distribution of the aortic chromaffin bodies is shown in Fig. 499. These bodies are numerous in the earlier months of foetal life; later there is a reduction in number, their function being taken over by the medulla of the adrenals. Some persist at the roots of the coeliac axis and superior mesenteric arteries. Although chromaffin cells arise from the blastema of the sympathetic system, yet they are differentiated before the nerve cells of that system, as if they represented the products of an earlier evolution. By their secretion they assist or serve as substitutes for the vasomotor sympathetic cells and for all nerve cells which have to do with regulating the action of nonstriated muscle.

In the master organ of the hormonal system, the pituitary body, the main secretory part is linked to a neural element; in the adrenal we meet with a linkage of a similar kind. The explanation of this association of neural and secretory elements still awaits formulation. In its functions the cortex of the adrenals is dominated by the pituitary.

The *Coccygeal Body* is a small mass of epithelioid cells situated on the ventral aspect of the coccyx. The cells are arranged round vascular channels, but are not neuroblastic in origin. Nerve fibres end in its peripheral capsule. Its function and origin are unknown [20].

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[2] For interstitial tissue, see Goddard, T. R., *Jour. Anat.*, 54, 173; Kingsbury, R. F., *Amer. Jour. Anat.*, 1914, 16, 59; Bascom, K. F., *ibid.*, 1923, 31, 223.

[3] Moszkowicz, L., *Zeitsch. Anat. Entwickl.*, 1936, 105, 37.

[4] For influence of oestrogens on inguinal and perineal structures, see Zuckerman

CHAPTER XXVIII

BODY WALL AND PELVIC FLOOR

Stages in the Evolution of the Body Wall.—Behind the apparently simple arrangement of structures in the body wall of man lies a long history, only some of the later stages being known to us [1]. Even in the lowest vertebrates the wall surrounding the pericardial and abdominal cavities is already muscular. We presume, however, that there has been a stage in which the body-wall was devoid of muscles, for in all vertebrates the myoblasts which give rise to the muscles of the body wall are derived from without. In fishes the musculature of the body wall is arranged in two systems: (i) a lateral or oblique system, in which the ribs are embedded; (ii) a ventral or longitudinal system, which extends from pharynx to tail. Both longitudinal and oblique systems are differentiated from one stratum. It is from a simple system of this nature that the musculature of the human body wall has been evolved (see Fig. 519).

Respiratory Stage.—With the evolution of lungs the musculature of the body wall assumed a respiratory function. In fishes its chief use—if one excepts the part it plays in body movements—is to assist in the circulation of the blood within the body cavity: to drive it on towards the heart, and to expand or contract the cavity as the alimentary canal fills and empties. By means of ribs embedded in the septa of the lateral wall of vertebrates above fishes, the musculature of the body cavity became capable not only of compressing or diminishing the body cavity, but also of expanding it, and thus filling the lungs with air. In this manner the body musculature entered into the service of the lungs, and

The ribs which served in the simple economy of the fish's body became strengthened and firmly jointed to the vertebrae; at the ventral ends of those encircling the lungs a supporting bar—the sternum—was evolved; the primitive sheets of musculature became differentiated to act on the ribs. In the latter part of the 2nd month, when the lungs and pleural cavities are undergoing rapid development, respiratory transformations similar in nature to those just mentioned are taking place in the human embryo.

etc., 1937, 24, 1 ; Long and Zuckerman, *Nature*, 1937, 139, 1106 ; Bourne, G., *Proc. Linn. Soc. N.S.W.*, 1936, 61, 221.

[17] See under note [15].

[18] Nicholson, G. W., *Jour. Path. Bact.*, 1931, 34, 711.

[19] For papers on chromaffin bodies: Swale Vincent and Curtis, *Jour. Anat.*, 1928, 62, 110 ; Bourne, G., see under note [15] ; Goormaghtigh, J. A., *ibid.*, 1936, 71, 76 (origin of paraganglionic tissue) ; Da Costa, A. C., *ibid.*, 1935, 69, 479 ; Kondratjew, N., *Ergcb. Anat.*, 1933, 30, 341 ; Koffmann, V., *Anat. Anz.*, 1937, 84, 120 ; Rosenthal and Willis, *Jour. Path. Bact.*, 1936, 42, 599 (chromaffin tumour with neurofibromatosis).

[20] Hollinshead, W. H., *Anat. Rec.*, 1942, 84, 1 (glomus coccygeum) ; Walker Sir J. Thomson, *Archiv. Mik. Anat. Entwickl.*, 1904, 64, 121.

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[17] See under note [15].

[18] Nicholson, G. W., *Jour. Path. Bact.*, 1931, 34, 711.

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[20] Hollinshead, W. H., *Anat. Rec.*, 1942, 84, 1 (glomus coccygeum) ; Walker Sir J. Thomson, *Archiv. Mik. Anat. Entwickl.*, 1904, 64, 121.

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Mammalian Stage.—We have already seen that the lungs of mammals develop within special cavities, which ultimately surround the heart; as the pleural cavities expand they dislocate from the neck and depress within the trunk a partition which completely separates the thorax from the abdomen. With the evolution of the diaphragm and the disappearance of the lungs from the abdominal cavity, the body wall musculature became further modified, so that it could control the movements of the thorax independently of those of the abdomen. The evolution of pleural cavities effected a transformation in the thoracic part of the body wall. The formation of the pleural cavities and the differentiation of the thoracic wall take place during the latter part of the 2nd month of human development.

Orthograde Stage.—It was formerly believed that the upright or orthograde posture is confined to man, and that it represents one of the more recently acquired human characters [2]. This is certainly not the case; man shares the orthograde posture with the group of primates with which he has so many structural affinities—namely, the anthropoid apes. Like man, they carry their bodies in an upright posture during progression. The smallest and most primitive of the anthropoid apes, the gibbon, is of ancient origin; the orthograde posture is therefore an adaptation which has been long established in the higher group of primates. With a change of posture from the pronograde to the orthograde, the action and fixation of the musculature of the body wall became greatly modified; the mechanism of respiration was necessarily altered. The chest became wide or barrel-shaped, the sternum broad; the heart came to rest on the diaphragm. The muscles of the abdominal wall had not only to carry on their respiratory function; they had also to support the abdominal viscera and to assist in emptying them. The mesenteric adhesions which take place during the early months of foetal life (see p. 407) are designed to give additional fixation to the viscera. The lower abdominal viscera came to rest on the pelvic floor; the muscles of the tail, which arise within the pelvis of pronograde mammals, were modified to form a muscular hammock for the support of the viscera and in the course of time the external tail became reduced to a coccyx. The caudal or coccygeal vertebrae are less robust in anthropoid apes even than in man. The spinal musculature and spinal column were altered to meet new postural conditions.

Plantigrade Stage.—If man shares the orthograde posture with a group of higher primates, the power of plantigrade progression is peculiarly his own. Everyone recognizes that the foot, the leg, the thigh of man have undergone extensive structural alterations, but the fact is often overlooked that the process of adaptation has also led to marked structural

changes in the body wall. The inguinal region especially has been modified. The great development and complete extension of the thigh have altered the musculature of the groin; the inguinal (Poupart's) ligament has been evolved. These structural adaptations have weakened the human groin and made it the commonest site of hernia. In the normal human upright posture the trunk is balanced on the pelvis; the crest of the ilium and the external oblique have become modified for this purpose. The muscles of the abdominal wall not only support the abdominal viscera, and maintain them during their respiratory excursions, but also take a part in producing and regulating the movements of the

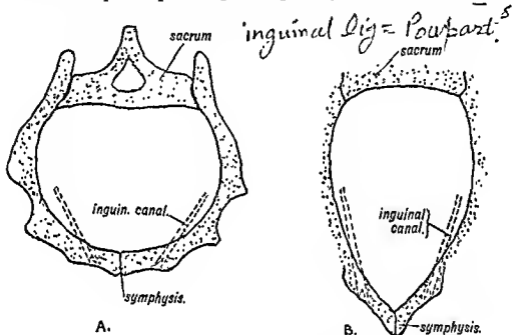


FIG 501.

- A. The Form of Pelvis and Inguinal Canal in Man
B. The corresponding forms in Pronograde Primates.

body Their functional value is often impaired in man, and hence he is the subject of those forms of slipping or dropping of the viscera which are grouped under the name of visceroptosis. He is liable to many other varieties of static disablements.

Inguinal and femoral hernia occur so rarely amongst mammals that they may be considered human peculiarities. Their frequency in man is due to certain structural changes in his pubo-femoral region, changes which have resulted mainly from his adaptation to upright progression. His susceptibility to hernia is due to [3]:

(1) The unique form of Poupart's ligament in man. It is scarcely developed in any other animals. In the orang, for instance—also an

Mammalian Stage.—We have already seen that the lungs of mammals develop within special cavities, which ultimately surround the heart; as the pleural cavities expand they dislocate from the neck and depress within the trunk a partition which completely separates the thorax from the abdomen. With the evolution of the diaphragm and the disappearance of the lungs from the abdominal cavity, the body wall musculature became further modified, so that it could control the movements of the thorax independently of those of the abdomen. The evolution of pleural cavities effected a transformation in the thoracic part of the body wall. The formation of the pleural cavities and the differentiation of the thoracic wall take place during the latter part of the 2nd month of human development.

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passage) is very much greater in man (A and B). In him, the most internal and this unfilled space forms the femoral hernia may escape. The formation of the femoral canal has, therefore, no embryological basis; it is not, like the inguinal canal, the site of an embryological outgrowth of peritoneum. The crural passage is relatively larger in women than in men, owing to the greater size of the female pelvic brim, and hence femoral hernia is much more common in women than in men. Some hint as to the method of treatment of hernia in man may be obtained from a consideration of the arrangement of structures that prevent them in other animals.

(v) Perhaps the most important factor in the causation of hernia in man is the compression to which the abdominal contents are subjected by the contraction of the musculature of the abdominal parietes during strenuous efforts, such as the lifting of heavy weights or the carrying of excessive burdens. Certain families are more liable to hernia than are others; oestrone, too, can soften the structures of the groin (see p. 533).

THE PELVIC FLOOR

Coccyx.—The retrograde changes undergone by the coccyx in the evolution of the human body are intimately connected with the formation of the pelvic floor. The coccyx in man is commonly composed of four vertebrae, more or less vestigial in nature, which represent the basal caudal vertebrae of tailed mammals. Evidence of their vestigial or retrograde nature is to be found in: (i) Only their centra are developed—with the exception of the first, which shows partial formation of transverse processes and neural arches (superior cornua). (ii) Delay in the appearance of the centres of ossification. These, instead of beginning in the 8th week as in a typical vertebra, commence after birth. The centre for the 1st coccygeal vertebra appears in the 1st year, that for the 4th vertebra about the 25th year; the 2nd and 3rd at intermediate periods. All four are fused into one piece about the 30th year. (iii) Late in life, between the 40th and 60th year, the coccyx unites with the sacrum.

The number of coccygeal vertebrae varies; four is the normal number, but there may be three or five. In embryos of the 7th week as many as eleven coccygeal vertebrae have been counted. The first coccygeal vertebra may join the sacrum, making six sacral vertebrae. The coccygeal vertebrae in anthropoids are more reduced as regards the development of their parts than in man.

The evidence of the former existence of a true tail in the ancestral

upright primate—the external oblique has no attachment to the crest of the ilium, and takes no part in forming the outer part of Poupart's ligament (Fig. 502), the aponeurosis from the lower muscular digitations terminating directly in the pillars of the external abdominal ring, thus strengthening the region of the inguinal canal. This is the usual termination in mammalia. In man the anterior part of the iliac crest has grown into the lower digitations of the external oblique and severed them from their tendinous fibres, which now form the main constituent of Poupart's ligament. The digitations thus inserted into the iliac crest help in balancing the body.

(ii) The internal oblique and transversalis (conjoined parts) in the orang, and in all primates except man, arise from the firm tubular

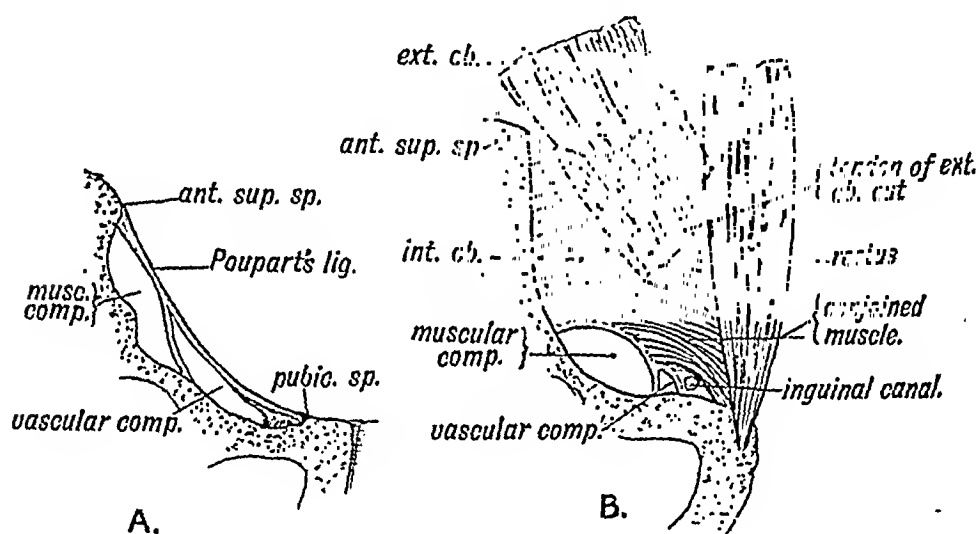


FIG. 502.

A. Poupart's (Inguinal) Ligament and the Crural Passage of Man.

B. Poupart's Ligament, Crural Passage and Sphincter-like Conjoined Muscle of the Orang.

sheath of the ilio-psoas, also from the extensive anterior border of the ilium, and, arching over the spermatic cord, end in a long insertion on the ilio-pectineal line. They act as a powerful compressor or sphincter of the inguinal canal, and thus prevent hernia (Fig. 502, B).

(iii) The human manner of walking and the great head of the human child at birth require a wide pelvis. All mammals adapted to the pronograde posture have a narrow pelvis, and hence a narrow anterior abdominal wall (Figs. 501, A and B) through which the inguinal canal passes very obliquely. The course of the canal is more direct in man, and therefore offers a great facility to the escape of the abdominal contents.

(iv) Owing to the width of his anterior abdominal wall, the size of the space between the edge of the pelvis and Poupart's ligament (the crural

The *Pelvic Floor* is peculiarly extensive in man, an adaptation to his upright posture. The floor is formed by the following structures : (i) The levator ani and its sheath (recto-vesical and anal fascia) on each side ; (ii) the coccyx and coccygeus muscles ; (iii) the constrictor urethrae (external sphincter) and triangular ligament ; (iii) the pyramiformis and its sheath may also be included.

Development of the Pelvic Floor.—The pelvic floor has been evolved in man by a transformation of the tail and the caudal muscles [6]. The arrangement of tail muscles in a four-footed mammal, such as the monkey or dog, is shown in Fig. 505, *A*, and the modification of this form



FIG 504 Newly born Child with Tail. (Drawn by R. H. Burne)

in anthropoids and man in Fig. 505, *B*. In mammals, two muscles, the pubo-coccygeus and ilio-coccygeus, act as depressors of the tail, the basal part of which plays the part of a perineal shutter ; in orthograde primates the tail no longer helps to close the perineum, its muscles serving in the support of the pelvic viscera. In pronograde apes these muscles are attached to the small V-shaped chevron bones on the under surface of the basal caudal vertebrae (Fig. 506). Another muscle, the ischio- or spino-coccygeus, acts as a lateral flexor of the tail. It is attached to the transverse processes of the caudal vertebrae, and arises from the dorsal border of the ischium. In man the pubo-coccygeus and ilio-coccygeus are blended into one sheet and form the levator ani. The shrinkage of the tail leaves the muscle partly stranded on the ano-coccygeal ligament

human stock consists of: (i) From the 5th to the 8th week the coccygeal region of the spine protrudes (Fig. 503) and the vertebrae number from 8 to 11; the notochord is traceable beyond the vertebral segments. (ii) Vestiges of the extensor and flexor muscles of the tail are frequently found (10% of bodies) on the dorsal and ventral aspects of the sacrum and coccyx. Occasionally small nodules of bone are found in front of the human coccyx, spanning the continuation of the middle sacral (caudal) artery; these nodules represent the chevron bones or haemal arches of tailed mammals. The depressors of the tail are attached to the chevron bones (see Fig. 505, A). (iii) True tails, consisting of external

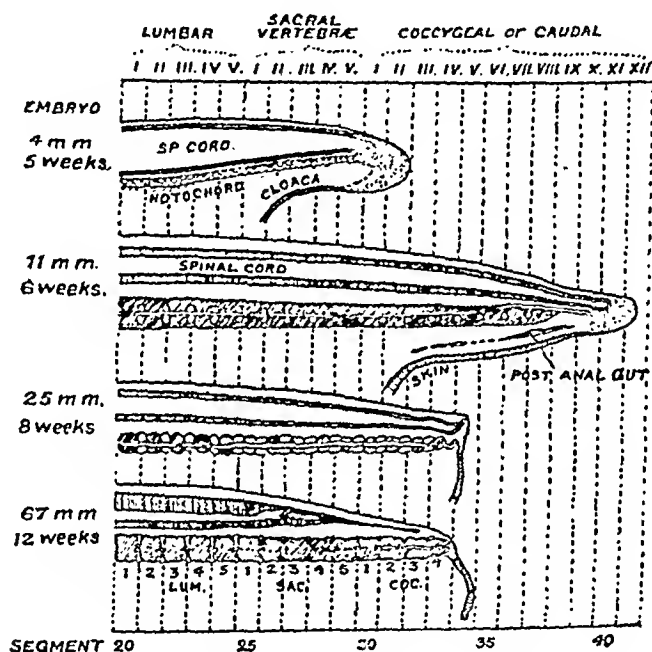


FIG. 503. The Rise and Retrogression of the Caudal Vertebrae during the 2nd and 3rd months of development. (After Kunitomo.)

prolongations of the coccygeal region, commonly fibrous, rarely containing vertebrae, occasionally occur [4]. (iv) The post-anal pit, always to be seen in the newly born child, marks the point at which the coccyx disappears below the surface early in the 3rd month. In man the coccyx forms part of the perineal floor. Instead of projecting far beyond the gut, as in tailed mammals, it terminates $1\frac{1}{4}$ inch above the anal canal.

Another piece of evidence has been discovered by Prof. Hammar [5]. As will be seen from Fig. 505, A, a slip of non-striated muscle, known as the *retractor ani*, unites the rectum to the ventral aspect of the coccyx. Prof. Håmmar found that a representation of this muscle is developed in connection with the rectum of the human foetus in the 7th week. It subsequently atrophies.

The *Pelvic Floor* is peculiarly extensive in man, an adaptation to his upright posture. The floor is formed by the following structures : (i) The levator ani and its sheath (recto-vesical and anal fascia) on each side ; (ii) the coccyx and coccygeus muscles ; (iii) the constrictor urethrae (external sphincter) and triangular ligament ; (iii) the pyri-formis and its sheath may also be included.

Development of the Pelvic Floor.—The pelvic floor has been evolved in man by a transformation of the tail and the caudal muscles [6]. The arrangement of tail muscles in a four-footed mammal, such as the monkey or dog, is shown in Fig. 505, *A*, and the modification of this form



FIG 504. Newly born Child with Tail. (Drawn by R. H. Burne)

in anthropoids and man in Fig. 505, *B*. In mammals, two muscles, the pubo-coccygeus and ilio-coccygeus, act as depressors of the tail, the basal part of which plays the part of a perineal shutter ; in orthograde primates the tail no longer helps to close the perineum, its muscles serving in the support of the pelvic viscera. In pronograde apes these muscles are attached to the small V-shaped chevron bones on the under surface of the basal caudal vertebrae (Fig. 506). Another muscle, the ischio- or spino-coccygeus, acts as a lateral flexor of the tail. It is attached to the transverse processes of the caudal vertebrae, and arises from the dorsal border of the ischium. In man the pubo-coccygeus and ilio-coccygeus are blended into one sheet and form the levator ani. The shrinkage of the tail leaves the muscle partly stranded on the ano-coccygeal ligament

(Fig. 505, *B*). Other fibres of the pubo-coccygeus lose their primary insertion to the coccyx, and become attached to the prostate, central point of the perineum, and to the anal canal. Both muscles, especially the ilio-coccygeus, retain in part their primitive attachment to the coccyx (cauda). The spino-coccygeus, or coccygeus muscle, is partly fibrous in man, its outer laminae forming the small sacro-sciatic ligament; its inner laminae remain muscular and form the coccygeus. In man, too, the origin of the ilio-coccygeus has sunk from the pelvic brim of the ilium

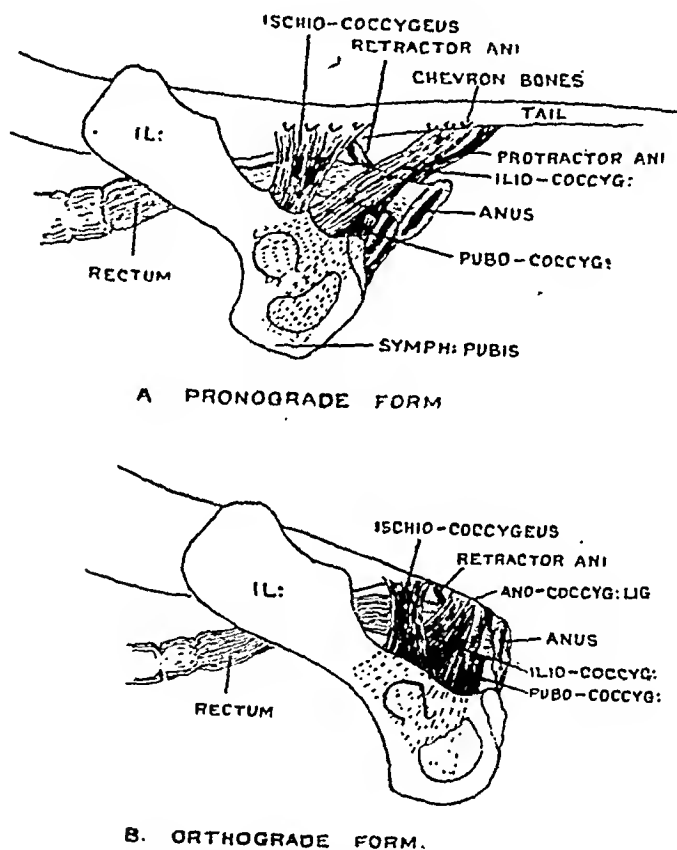


FIG. 505. Diagram to show the Pelvic Muscles of a Pronograde Ape (*A*) and of an Orthograde Ape (*B*).

on to the obturator fascia; traces of the primitive origin from the pelvic brim can often be detected (Fig. 507). The white line, a structure peculiar to man, marks the new point of origin of the levator ani from the obturator fascia. The "white line," which is not depicted in Fig. 507, strengthens the origin of the levator ani from the obturator fascia.

In fishes (selachians) the levator ani is represented by a backward continuation of the rectus abdominis (Paramore). The pelvic part of the rectus ends in the tail; anteriorly it is attached to the movable pelvic girdle. The cloaca of the dog-fish passes out between the right and left

primitive representatives of the levator ani, which can compress the cloaca not by depressing the tail, as in mammals, but by pulling the pelvis backwards.

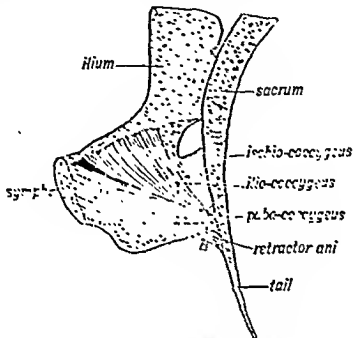


FIG. 506. The Pelvic-canal Muscles of a Monkey.

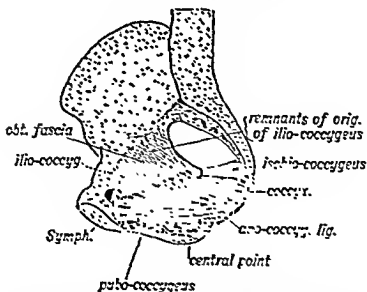


FIG. 507. The Pelvic Muscles of Man—corresponding to those shown in Fig. 506.

Pelvic Fascia and Fasciae in General.—It has been customary to regard fasciae as separate structures forming distinct sheets with devious and complex courses. It is possible by dissection to prepare and display them according to accepted descriptions, but the structures so displayed are

artificial and not the true structures which the surgeon or physician has to deal with in actual practice. Embryology is the best guide to their nature. Take, for example, the development of the fasciae seen on making a section of the upper arm (Fig. 508). When the limb-bud appears, which it begins to do about the end of the 4th week of development, a section through it reveals a syncytium of mesodermal cells [7], the blastema of bones, muscles, etc., surrounded by a covering of ectoderm (Fig. 509). Very soon the central cells of the bud are densely grouped and form the basis of the skeletal axis. Other cellular constituents of the blastema arrange themselves to form the biceps, triceps

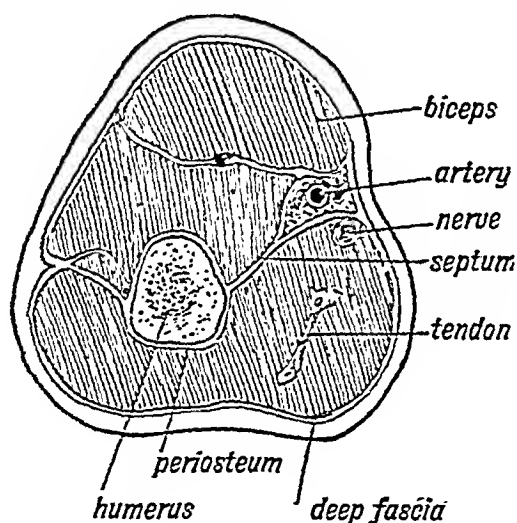


FIG. 508.

FIG. 508. Section across the Upper Arm to show the continuity of its Fascial System.

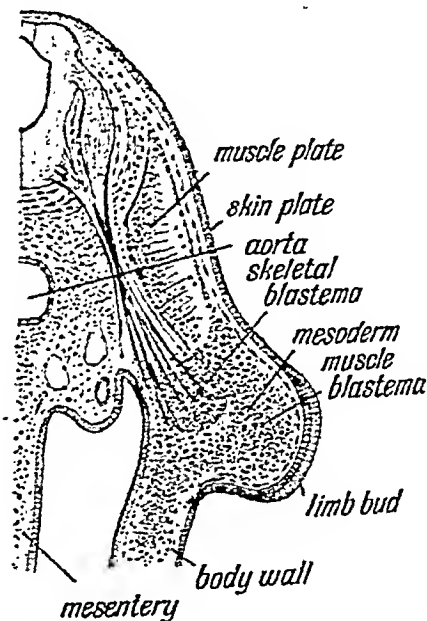


FIG. 509.

FIG. 509. Section of a Limb-bud to show the manner in which its Tissues become differentiated. (After Kollman.)

and muscles of the arm; other cells become the walls of vessels and the sheaths of nerves. After these various groups of cells have become differentiated, there is left over a cellular residue in which the highly differentiated cell-groups are enmeshed. The undifferentiated mesoderm forms the connective tissue or fascial system of the part. From the manner of its origin it is evident that the connective tissue system—the fasciae and septa—must form a continuous sponge-work of sheaths, each being in continuity with that of every surrounding structure. The sheaths of the biceps, triceps and brachialis anticus, the periosteum of the humerus, the deep fascia, internal and external intermuscular septa, the sheaths of the vessels and nerves of the arm, represent the mesodermal tissue which was left over after the individual structures of the brachium

were differentiated, and are, from the manner of their origin, necessarily in continuity (Fig. 508). They can only be artificially separated from each other. It is more accurate and easier to describe fasciae, then, not as separate structures but as adjuncts of the structures which they surround or ensheath.

As to the manner in which *connective tissue* is developed, there are two opinions: (i) that the substance of the cell body elongates and forms a fibre; (ii) the more probable, that fibres are formed in a ground substance (gel) which lies outside the cell body, but is under the influence of the cell [8].

The **Pelvic Fascia**, which strengthens the pelvis floor, is composed of the sheaths of four muscles: (i) Levator Ani; (ii) Obturator Internus; (iii) Piriformis; (iv) Constrictor Urethrae and deep Transversus Perinei. The fibrous capsules of the following viscera also form part of it: (i) Prostate and Vesiculae Seminales in the male; (ii) Vagina and Uterus in the female; (iii) Bladder; (iv) Rectum. Under the title of pelvic fascia these eight elements are combined. To these must be added the important sheaths of the vessels—especially of the vesical, uterine and perineal arteries.

I. The *Obturator Fascia* is the sheath on the inner or pelvic aspect of the obturator internus; the sheath on the outer side of the muscle is formed by the periosteum and obturator membrane. The obturator fascia is attached at the circumference of the muscle. There it becomes continuous with the periosteum of the os innominatum. The part above the white line (supra-linear) is intra-pelvic; the part below (infra-linear) is perineal and situated on the outer wall of the ischio-rectal fossa.

II. *Recto-vesical and Anal Fasciae*.—The levatores ani form a muscular floor for the pelvis, stretching from the white line of one side to the white line of the other. The sheath on their under surface—on the inner wall of the ischio-rectal fossa—forms the anal fascia. On the upper surface their sheath forms the greater part of the recto-vesical fascia. The pelvic viscera rest on the upper surface of the levatores ani and the capsules of the viscera are continuous with the sheath on the upper surface of the muscles. The combined visceral capsules and upper sheath of the levatores ani form the recto-vesical fascia.

III. The *Triangular Ligament* is situated in the neighbourhood of the constrictor urethrae muscle (Fig. 510), but it can scarcely be regarded as its sheath. It is rather a fibrous septum which on its deep or pelvic aspect gives attachment to the prostate and to the bulb and root of the penis on its lower or perineal aspect. The inferior transverse fibres of the constrictor form really a separate muscle—the deep transverse

perineal—a derivative of the sphincter cloacae (sec p. 543). The apex of the prostate rests on the muscle, its fibrous capsule being continuous with the posterior layer of the muscle sheath—the deep layer of the triangular ligament.

IV. The inner sheath of the pyriformis forms the *pyriform fascia*. The coccygeus is continuous with the levator ani and its sheath forms part of the recto-vesical fascia. The loose perirectal sheath is also continuous with the tissue of the fascia pyriformis. The laxity of the connective tissue which binds rectum, bladder and uterus to the pelvic fascia is evidence of the mobility of these organs. As they fill and empty, they must be free to move.

The pubo-prostatic ligaments and the lateral vesical ligaments are

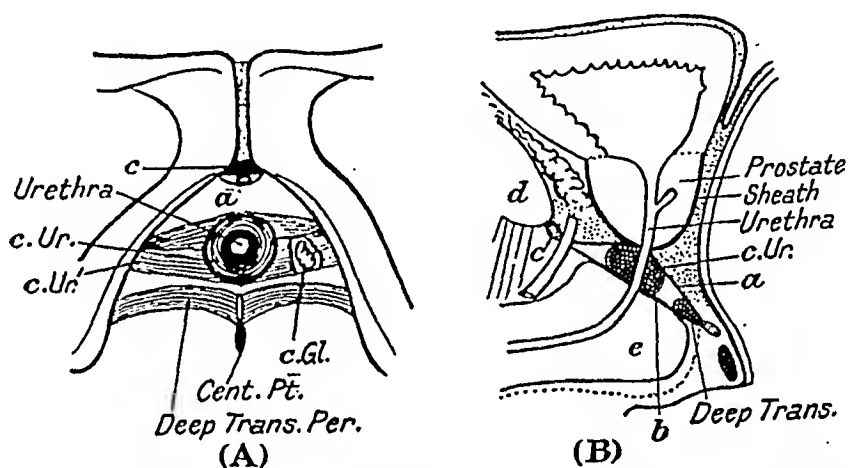


FIG. 510.

- A. The Constrictor Urethrae with attachments to the Subpubic Arch. *c. Ur.*, circular fibres; *c. Ur'*, transverse fibres; *deep-trans. per.*, deep transverse perineal muscle; *Cent. pt.*, central point of perineum; *c. Gl.*, Cowper's gland exposed; *a*, deep layer of triangular ligament; *e*, subpubic ligament. (A. J. E. Cave.)
- B. The Constrictor Urethrae and Triangular Ligament as seen in sagittal section. *a*, deep layer of triangular ligament; *b*, anterior layer; *e*, subpubic ligament; *d*, symphysis pubis; *e*, bulb; *deep trans.*, deep transverse perineal muscle. (A. J. E. Cave.)

strengthened parts of the fibrous capsule of the prostate, which provide the bladder with a pubic fixation. The vesical musculature, in emptying the bladder, acts from the pubic fixation thus obtained. The great strains to which the pelvic vessels are exposed when the pelvic floor and viscera are depressed in forced muscular efforts render a strong fibrous protective vascular sheath necessary. Hence the tough fibrous coating round the uterine and vesical vessels. Alcock's canal is formed from the fibrous sheath round the pudic artery and nerve (Elliot-Smith).

Cervical Fascia.—From what has been said of the pelvic fascia, the nature and arrangement of the cervical fascia will be readily understood. It is composed of (*i*) the sheaths of the cervical muscles (sterno-mastoid,

etc.); (ii) of the sheaths of vessels (carotid sheath, etc.); (iii) the sheaths of nerves (axillary sheath, etc.); (iv) the fascial capsules of viscera, such as the thyroid body, salivary glands, and pharynx. The carotid sheath and sheaths of the great vessels extending from the base of the skull to the pericardium within the thorax are formed to a great extent from mesodermal tissue that was developed within the visceral arches of the pharynx. At first the pericardium lies beneath the mouth and pharynx. With the development of the neck at the end of the 2nd month of foetal life, the cervical structures and their sheaths become stretched, but they maintain the ancient connection between skull base and pericardium [9].

Peculiar Fasciae.—The muscular sheaths on the inner aspect of the transversalis, iliacus and psoas also have been regarded as forming distinct fasciae. On the other hand, some fasciae are quite discrete structures. The *palmar fascia* is part of the palmaris longus muscle; the plantar, part of the plantaris muscle; the vertebral aponeurosis or fascia, part of the layer of muscle which is represented by the serratus posticus superior and inferior; the epicranial aponeurosis is part of the platysma sheet. The middle layer of the lumbar fascia represents a primary septum developed between the dorsal and ventro-lateral groups of musculature (see p. 109).

Fascial structures have also a distinct relationship to the *lymphatic system*. Lymphatics follow the septa and capsules of glands and muscles; the lymphatics of the lung collect in the connective tissue separating its lobules. The most remarkable of all the capsular tissues of the body are those represented by the membranes of the central nervous system; there the cerebro-spinal spaces, or clefts, have separated the cerebral capsule into three layers—the pia mater, arachnoid and dura mater (see p. 201).

Sir Leonard Hill has also drawn attention to the part which ensheathing fasciae play in assisting the circulation of the blood. Every contraction of the muscles of the thigh tends to force the venous blood within the sleeve formed by the fascia lata on towards the heart.

Body Wall.—Having thus traced the evolution of the pelvic floor and discussed the nature of fasciae generally in connection with the pelvic fascia, we pass on to consider the development and nature of the abdominal and thoracic walls.

Bilateral Symmetry of the Body.—From a developmental point of view the body is made up of two symmetrical halves: each half of the embryonic plate, taking the medullary groove as the line of division, contributes equally to the formation of the body. Each produces a half of the nervous system, each a half of the vascular, muscular and alimentary

systems, so that each individual is in reality made up of two halves, right and left, of identical origin. Although the right side of the body rises from the same blastocyst as the left, yet each becomes specialized structurally and functionally, so that as development goes on there appears a very remarkable asymmetry. Even in the papillary patterns of the hands and feet there are standard right-sided and left-sided forms (see p. 653).

Ventral Line of the Body.—The structures which are contained within

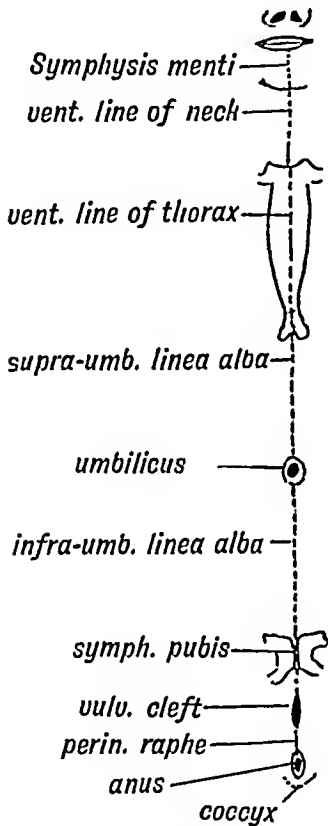


FIG. 511.

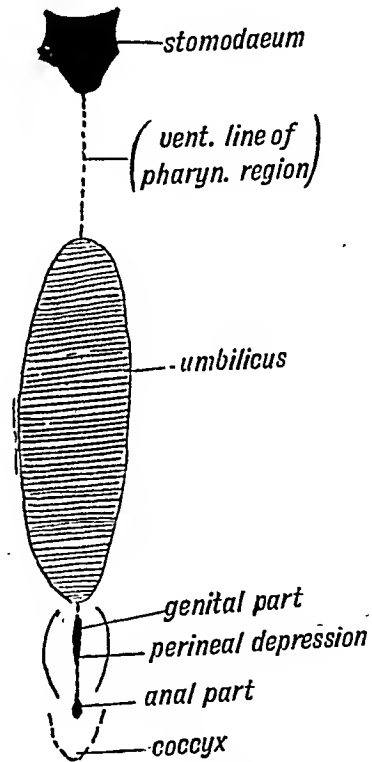


FIG. 512.

FIG. 511. Diagram of the Structures formed in the Median Ventral Line of the Body.

FIG. 512. The Median Ventral Line in an Embryo of 4 weeks, to contrast with the corresponding line in the Adult.

the right and left body walls become united along the *ventral line* from the mouth to the anus (Fig. 511). The mesoderm, muscle plates, dermatomes, nerves and cartilaginous outgrowths, which are produced on each side of the median dorsal line of the body, meet along the median ventral line. In this line are developed the symphysis of the lower jaw, the body of the hyoid bone (copula), the white line of the neck and angle of the thyroid cartilage, the sternum, the supra-umbilical part of the linea alba, umbilicus, infra-umbilical part of the linea alba, symphysis pubis, the septum of the penis, and of the scrotum and perineal raphe.

The ventral line is continued forwards on the face between the parts derived from the right and left mesial nasal processes.

The idea was at one time prevalent that the whole of this line was formed by the fusion of one somatopleure with the other; the median ventral line was the suture formed by the union. Such is not the case. The blastoderm, which lies at first like a cap on the yolk sac (Fig. 21), is produced or folded anteriorly to form the fore-gut and the part of the body above the umbilicus; it is produced posteriorly to form the hind-gut and the part of the body below the umbilicus. In an embryo, at the commencement of the 4th week, the greater part of the ventral line

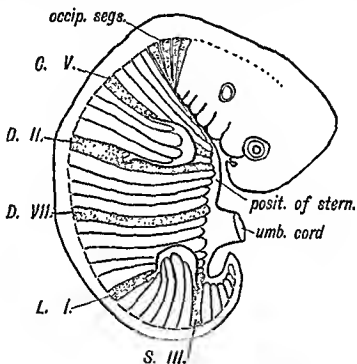


FIG. 512.

is occupied by the umbilicus (Fig. 512). At that time the umbilicus is 3 mm. in diameter, the entire ventral line being about 4 mm. At the end of the 7th week the ventral line measures 15 mm.; the umbilicus retains its former size, about 3 mm. [10]

At first the somatopleure shows no trace of segmentation. The paraxial masses of mesoderm become segmented in the 4th week and form muscle plates (Fig. 84). From each muscle plate [11] of the primitive segments a process grows down into the somatopleure (Fig. 513). The somatopleure thus becomes segmented secondarily, the process of

segmentation spreading from the dorsal to the ventral side of the plate, but along the median ventral line of the body wall, a band of the primitive mesodermal tissue remains unchanged and undifferentiated. In the ventral band between the left somatopleure and the right are formed the sternum and the linea alba (Fig. 511). In lower vertebrates, in fishes, and to a less marked extent in amphibians and reptiles the myotomic segments remain distinct from end to end of the trunk. That part of the ventral median line which extends from the umbilicus to the anus represents the site of the cloacal membrane—a purely epithelial structure. We have seen how the suprapubic part of the cloacal membrane is invaded by the mesodermal tissues on each side of it and how the condition known as ectopia vesicae results if this invasion of the ventral median line is arrested (p. 544).

Formation of Ribs.—Ribs, like all true skeletal bones, pass through three stages [12]: (i) They are represented by a mesenchymatous or membranous basis in the fibrous tissue (septa) between the muscular segments of the somatopleure (Fig. 513). The condensation of the costal mesenchyme appears at the beginning of the 5th week as a separate vertebral element. (ii) The mesenchymatous basis or *blastema* of the rib becomes cartilaginous. (iii) Periosteal ossification over the cartilage follows by the end of the 7th week, but the process of ossification leaves the ventral parts of the costal segments untouched; they form the costal cartilages; in lower forms they become ossified and form sternal ribs. The process of chondrification begins at the dorsal end of the ribs in the 6th week, and spreads ventrally, thus repeating the order in which the blastema was laid down. The extension ventralwards of the ribs corresponds with the growth and expansion of the lungs; at the beginning of the 7th week the ribs scarcely reach the lateral or axillary line of the body, but by the end of this week they have effected a junction with the sternal bars (Fig. 517). The ribs from the 1st to the 7th are developed in the somatopleure over the pericardium. In lower vertebrates, such as reptiles, each rib articulates with the neural arch of a vertebra by two heads, dorsal and ventral (Fig. 78). The tuberosity of a rib represents its dorsal head. In man, with the exception of the first and last rib, or in some cases the last two ribs, the costal head is placed opposite an intervertebral disc. The bodies of vertebrae arise from adjacent parts of two segments; they are intersegmental in position, whereas discs are intrasegmental. Ribs are also intersegmental—all save their heads—which are intrasegmental in origin (p. 98). In the case of the 1st rib the head has shifted backwards to the body of the 1st vertebra, while in the 12th and sometimes the 11th, the head and tuberosity are fused, and both costal processes

articulate with the part of the vertebra which represents a transverse process.

The Sternum.—In man and anthropoids the sternum has become flat and highly modified owing to certain alterations in the shape of the thorax (Fig. 435). With the adaptation to the upright posture the thorax becomes flattened from back to front; its transverse diameter is as great, or greater, than the antero-posterior. The type of respiration is greatly altered. The sternum also becomes wider and shorter. To understand the nature of this change it is necessary to note the characters of the sternum of a pronograde mammal, such as the dog or ape (Fig.

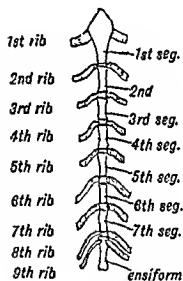


FIG. 514.

FIG. 514. The Form of Sternum in a Pronograde (quadrupedal) Mammal.

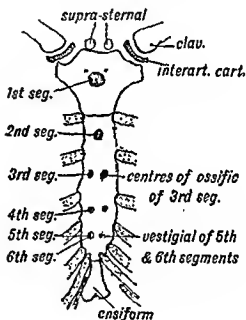


FIG. 515.

FIG. 515. The Form of Sternum in a Mammal adapted to the Orthograde (upright) Posture. The Points of Ossification are also shown.

514). In such, the sternum is typically made up of seven segments: 1. A modified anterior segment, the *pre-sternum*. 2. Five narrow, cylindrical segments or *sternebrae*, forming the *body* of the sternum. 3. The *ensiform process*, a hind segment, complex in nature and ending in the mid ventral line. The ensiform process frequently bifurcates, but is never segmented.

The characters which distinguish the human sternum are: 1. Each segment is flat and wide; 2. the segments of the body fuse together

during the years of adolescence, the fusiform beginning behind and passing forwards; 3. the 4th sternabra of the body is usually vestigial and is probably made up of two or more fused segments [13].

In low primates 8 or 9 pairs of ribs may reach the sternum, six or more sternebrae being then present [14]. In man the number has been reduced to 7 pairs, the sternal ends of the 7th pair lying in front of the 4th sternabra. It is not uncommon to find the 8th rib reaching the sternum, especially on the right side; it is rare to find the 7th pair fail to reach the sternum. The more frequent presence of an 8th sternal rib on the right side is due to right-handedness (Cunningham) or, as seems more probable, to give a more secure origin to the right costal fibres of the diaphragm,

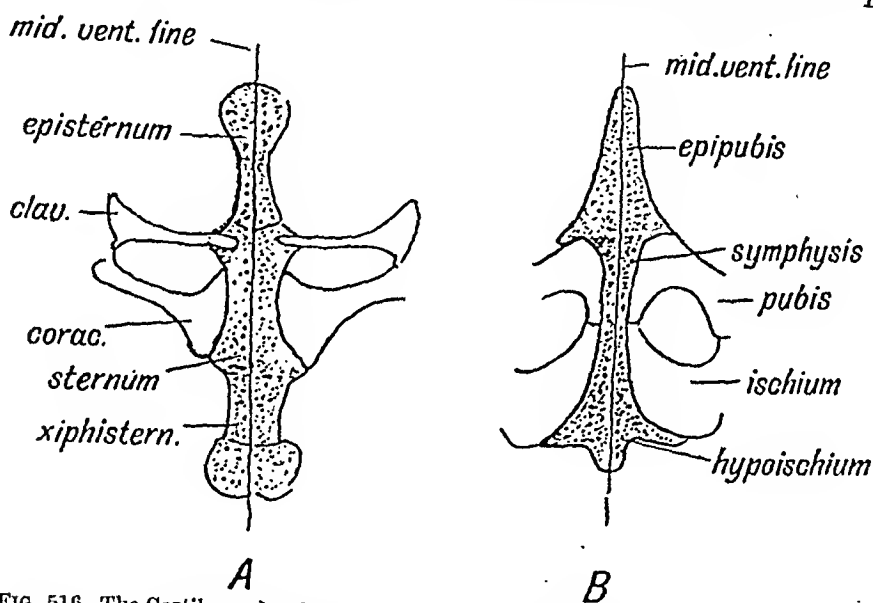


FIG. 516. The Cartilages developed on each side of the Median Line between the Shoulder and Pelvic Girdles. *A*, the shoulder girdle of the frog; *B*, the pelvic girdle of sphenodon. (The term "epi-sternum" is wrongly applied in Fig. *A*; it should be omo-sternum or supra-sternum. There is now a general agreement that the term epi-sternum should be reserved for the membrane bone formed between the clavicles.)

which have a greater resistance to overcome during inspiration than those of the left side. In man and the anthropoid apes a new feature appears in the lower costal cartilages [15]. The 5th, 6th and sometimes the 7th throw out processes which articulate with the cartilage below. When, during inspiration, the diaphragm raises the chest, these articulations permit it to elevate the 5th and 6th pairs of ribs as well as the 7th pair.

Morphology of the Sternum.—In amphibia the ventral parts of the shoulder and pelvic girdles develop towards the ventral median line. In the median line a rod of cartilage is formed between them (Fig. 516). The median rod is differentiated as right and left bars from the ventral parts of the limb girdles [16]. The right and left bars fuse to form the

median cartilage. The median rod between the shoulder girdles becomes the sternum; it is divided into three parts—*anterior*, which projects in front of the girdle (*omo-sternum* or *supra-sternum*); *posterior*, behind the girdle; and the *middle*, with which the shoulder girdle articulates (Fig. 516, *A*). The sternum affords a basis from which muscles act on the shoulder girdle, and also a ventral basis for the articulation of the shoulder girdle. In all classes of vertebrates, the sternum is developed over and shields the heart. The median cartilage of the pelvic girdle is similarly divided into *anterior*, *middle* and *posterior* parts (Fig. 516, *B*).

The evolution of a costal type of respiration in reptiles leads to a further stage of sternal development. Some of the costal processes of the vertebrae grow towards the median ventral line, some of them reaching and articulating with the middle part of the bar between the shoulder girdles; this part now serves as a fulcrum or sternum for both ribs and girdle. Such a condition is also seen in birds and monotremes (Fig. 541). In higher mammals the ventral part of the shoulder girdle retains its ventral connection with the sternum only through the clavicle; the sternum still serves as the basis of origin for muscles which act on the shoulder girdle and on the arm. Its chief purpose has become respiratory. In the human sternum the three parts of the primitive sternum can be recognized: the *supra-sternal bones* (Fig. 515), which are only rarely separated from the *presternum* [17], represent the *anterior part* (*omo-sternum* or *supra-sternum*); the *manubrium* and *body*, the *middle part* of the shoulder girdle sternum; and the *ensiform process*, the *posterior part*.

Development of the Sternum [18]. In Fig. 517 four stages in the development of the human sternum are represented. Stage *A* shows the extent to which the ribs have become chondrified at the end of the 6th week; the cellular costal blastema, into which the process of chondrification is spreading, is not shown. In the following week (Stage *B*) the process of chondrification has reached the middle line in the region of the manubrium. The ventral ends of the ribs are now joined together by a ventral or lateral sternal bar. The sternal bars in the region of the presternum have begun to fuse together across the middle line. At their anterior extremities the sternal bars are joined by the ventral cartilaginous ends of the clavicles. In the presternum or manubrium there is thus an element in each side derived from the ventral end of the clavicle. In Stage *C*, about the end of the 8th week, the process of fusion is advanced, but the projection of the foetal heart and liver at this time (see Fig. 61), tends to keep them apart. Each sternal bar has now 7 ribs continuous with it, and its posterior end is free

Early in the 3rd month (Stage *D*) the process of fusion is complete, the cartilaginous basis of the sternum has been formed by the fusion of right and left bars. At the end of the 2nd month the diaphragm is descending to its final position, the pleural cavities are rapidly forming and the liver is assuming a more abdominal position. Charlotte Müller [19], whose illustrations are represented here, found that the mesenchymal sternal bars were chondrified as direct extensions from the ribs.

The sternum is thus developed in the median ventral line over the

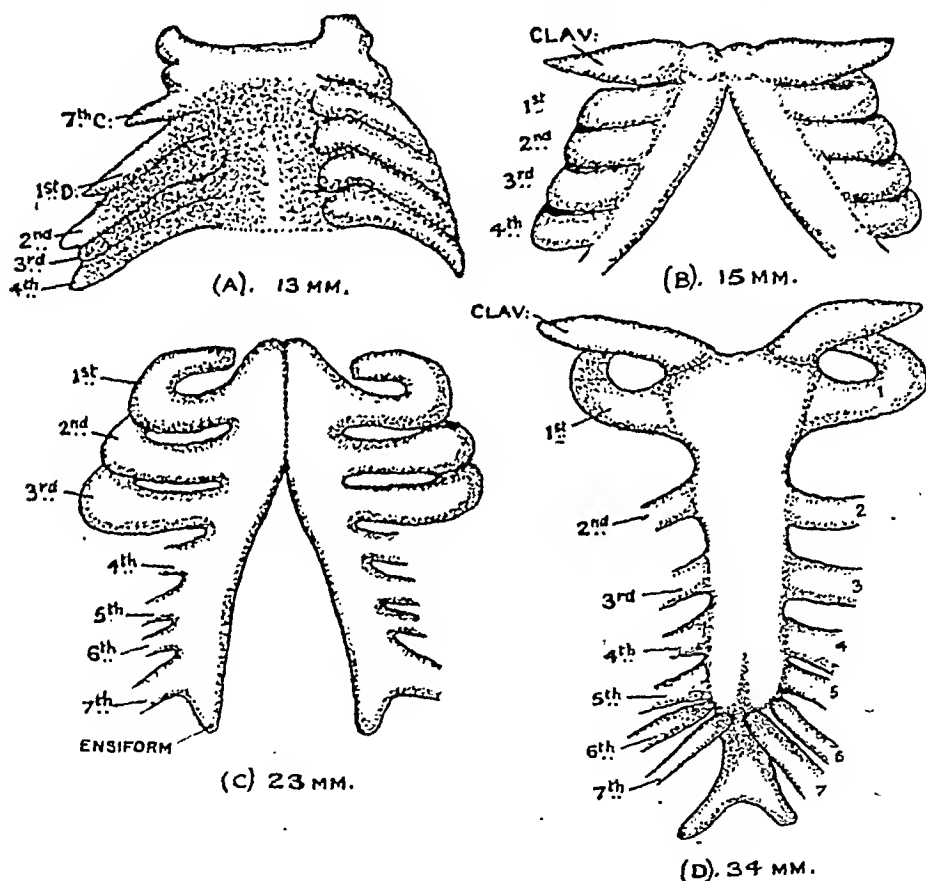


FIG. 517. Four stages in the Chondrification of the Human Ribs and Sternum and showing the Fusion of the Sternal Bars. (After Charlotte Müller.) *A*, end of 6th week; *B*, end of 7th week; *C*, end of 8th week; *D*, end of 10th week.

pericardium and between the mandible in front and the umbilicus behind (Figs. 511, 513). The mesoderm condenses during the 5th week on each side of this part of the median line to form the right and left mesenchymal bars of the sternum, which anteriorly are continuous with the bases of the ventral part of the shoulder girdle (Fig. 518). The right and left *mesenchymal sternal bars* fuse gradually in the middle line, the process of fusion commencing at the presternum and spreading backwards.

The sternum was regarded by Paterson as a structure arising independently of the ribs on each side of the median ventral line, a view which has been substantiated by all later investigations. The other view is that each sternal bar is produced from the ventral ends of the ribs, each rib contributing a segment to the bar. The evidence of comparative anatomy and the difference in the type of the cartilage cells in the costal and sternal elements negative such an interpretation. On the other hand, all recent investigators are agreed that the manubrium sterni develops in a distinctive manner and contains at least one element derived from the shoulder girdle [20].

In its development the sternum passes through three stages—fibrous,

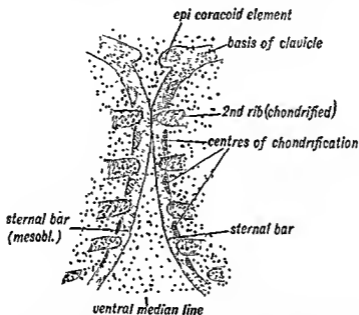


FIG 518. The Sternal Bars in an Embryo of 7 weeks. The element, here marked "epi-coracoid," represents the element which the shoulder girdle contributes to the manubrium. The proper name for this element is still unsettled. (After Paterson.)

cartilaginous and bony. 1. *Fibrous or Mesenchymal Stage*.—In the 7th week (Fig. 518) the costal cartilages are already chondrified. The mesoderm on each side of the median line, in which they end, has become condensed, and forms the membranous basis of the two sternal bars (Paterson). The bars begin to fuse together anteriorly. 2. *Cartilaginous Stage*.—The blastema of each sternal bar begins to chondrify in the intervals between the ends of the costal cartilages. The processes of chondrification and fusion proceed apace, and by the commencement of the 3rd month the segments of each side have united to form the cartilaginous sternal bars (Paterson). Fibrous joints are subsequently formed between the presternum and mesosternum and between the

mesosternum and ensiform process. A fibrous and then synovial joint is also developed at the union of the costal cartilages with the sternum (6th month foetal life), except in the case of the 1st pair, where a synovial joint is only occasionally present. 3. *Ossification*.—A centre appears for each sternebra; those for the 3rd and 4th of the mesosternum are frequently double, one being placed on each side. The centres for the 4th mesosternal segment may not appear. The centre for the presternum (there may be two or even more) appears about the 4th month; the centres behind appear in the 6th and 7th month; that for the 4th sternebra of the mesosternum appearing about the time of birth [13]; that for the ensiform in the first year after birth. The process of fusion of segments begins behind about puberty; the segments of the mesosternum are united together by the 25th year. Occasionally a median foramen may be seen in the sternum; it is due to imperfect union of the sternal bars.

The **Sterno-Manubrial Joint** becomes of great functional importance in man and those primates adapted to the upright posture [21]. Even in old age this joint is rarely ossified (8%, Paterson). In man a considerable respiratory movement occurs between the manubrium and body of the sternum. The manubrium moves in continuity with the ventral ends of the 1st pair of ribs; the body of the sternum follows the excursion of the 3rd to the 7th pairs of sternal ribs. As a rare abnormality (commoner in black than in white races) this joint is formed between the 1st and 2nd segments of the mesosternum [22].

Linea Alba.—The separation of the sternal bars does not represent an ancestral phase, but has arisen during developmental life to accommodate, first the yolk sac and later the large heart and liver of the embryo. In Fig. 519 is shown the early condition of the linea alba—from the classical research by Bardeen and Lewis [23]. The umbilical cord is still distended by a loop of intestine, and the two recti are wide apart, separated by the medial ventral membrane—the *primitive linea alba*. The two sternal bars are also held apart by the condition of the umbilical structures; indeed, the primitive linea alba is not only wide, but also extends from the neck to the perineum. In the 10th week there is a marked elongation of the lumbo-sacral region of the spine; the intestines return from the umbilical cord to the abdomen, the chest wall expands before the growing lungs and the mesial ventral line becomes gradually narrowed.

In Fig. 520 a transverse section is shown of the muscular layers in the anterior or thoracic body cavity of a lizard, and which also represents a stage in the evolution of the musculature of man's body wall [24]. It will be seen that there are three layers: an outer represented by the

rectus and external oblique; an inner by the transversalis, and a middle double layer—the internal and external intercostals. In the abdomen both strata of intercostals are combined in one layer—the internal oblique. The three layers are functionally different; the transversalis is a constrictor of the body cavity; the middle layer is mainly respiratory in its action; the outer is also respiratory, but chiefly concerned in body movements. The musculature of these three layers is developed in the somatopleure, and is apparently derived from the primitive segments (see p. 579). An abnormal muscle, the *sternalis*, is present



FIG. 519.

FIG. 519 The Primitive Linea Alba in a Human Fetus in the 8th week—20 mm. long. (After Bardeen and Lewis) Only the right half of the body is shown, the rectus abdominus is lateral in position, it and the sternal bars being kept from the mesial ventral line by the structures in the neighbourhood of the umbilicus

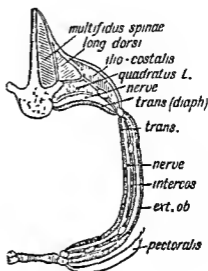


FIG. 520.

FIG. 520 Transverse section of the Thoracic Wall of a Lizard to show the Primitive Arrangement of the Muscular Strata of the Body Wall

in 6% of bodies [24]; it lies superficial to the origin of the pectoralis major and is derived from the primitive rectus sheets.

Development of Voluntary Muscle.—Although the evidence of comparative anatomy justifies us in believing that the cells which give rise to voluntary muscles in the somatopleure of the body wall and in limb-buds are derived from the muscle plates of the primitive segments, yet the actual migration in the embryo has not been proved. Nor is the proof easy, for at an early stage the cells (myoblasts) which are to give rise to muscle fibres are indistinguishable from those which will give

on its surface; the fibres, with unchanged cytoplasm round their nuclei, have become enclosed in a special sheath—the sarcolemma. surrounding cells by their protoplasm assuming a striated appearance—the striae being confined to the periphery of the cell, the nucleus remaining central (Fig. 521, *A*). By the beginning of the 4th month myoblasts have become elongated; they are now multinucleated, the nuclei being arranged along the core of the cell—within the striated cortex [25]. A cell is thus transformed into a fibre as a result of repeated nuclear divisions being unattended by division of the cell body. Fibres retain an end to end union. At the beginning of the 5th month of development the embryonic fibres undergo a further radical change. The nuclei are no longer arranged along the core of the fibre, but have moved to a position on its surface; the fibres, with unchanged cytoplasm round their nuclei, have become enclosed in a special sheath—the sarcolemma.

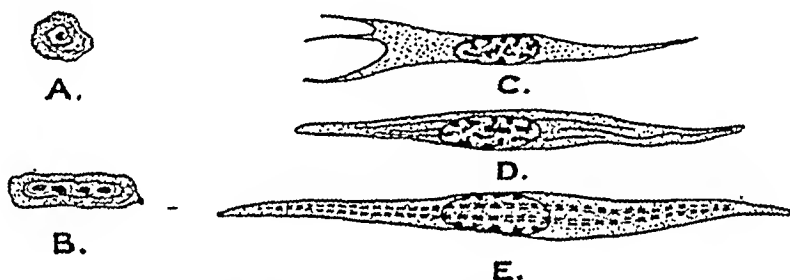


FIG. 521. *A*, Myoblast from a Human Embryo in the 7th week of development (E. Hewer); *B*, the same in the 9th week (E. Hewer); *C*, *D*, *E*, three early stages in the differentiation of a myoblast (Godlewski).

Myoblasts undergo differentiation whether nerve fibres reach them or not. Towards the end of the 3rd month (11th week) nerve fibres reach the developing myoblasts; it is then that striation appears in their fibrillae and motor end plates are formed (Cuajunco). Myoblasts cease to divide and to give rise to new fibres after the 4th month [26]. Yet when a fully-grown fibre of an adult is injured repair is effected by the nuclei of the injured fibre dividing and redividing until the defect is made good. After birth muscle fibres grow in size but not in number. Lockhart and Brandt observed, in a foetal sartorius which was 5 mm. long, that a fibre extended from end to end of the muscle; this is also the case in an adult sartorius, where fibres may have a length of 400 mm. A fibre can contract to less than half of its resting length (Haines). Tendon fibres are developed in the same way as myoblasts, only they contain no myoplasm.

Muscle Spindles.—These intra-muscular sensory bodies, which Sir Charles Sherrington discovered in 1894, become differentiated in the 9th week—at first being indistinguishable from other myoblasts. The

myoblasts which are to become muscle spindles undergo the same changes as other myoblasts, except that they stop short at the stage where their nuclei are arranged centrally. In the 3rd month a capsule is formed round the spindle on and in which both sensory and motor nerves terminate, for spindles retain the power of contractility [27].

Embryonic cells of all kinds have the power to contract and to move. This power becomes enhanced in muscle cells by the provision of a special structure. Prof. Eben Carey, by subjecting the musculature of the bladder to recurrent stresses, has caused plain muscle cells to assume a striated structure [28].

How the growth of muscles is regulated so that they extend at the same rate as the bones, skin, arteries and nerves which lie beside them is not known. Dr. Wheeler Haines is of opinion that bones serve as pacemakers in growing limbs [29].

NOTES AND REFERENCES

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[2] Keith, Sir A., see under note [1].

[3] *Comparative Anatomy of the Pelvis*, 1915, p. 189 (liable to hernia). For influence of oestrogens on tissues of inguinal region, see references in note [6], Chapter XXVII. For dimensions and shape of English pelvis, see Nicholson, C., *Jour. Anat.*, 1945, 79, 131, 503.

[4] For accounts of tailed children, see Harrison, R. G., *Johns Hopkins Hosp. Bull.*, 1901, 12, 96; Reynolds, R. J., *Brit. Jour. Radiology*, 1932, 5, 457 (occult tails); Keith, Sir A., *Nature*, 1921, 106, 845; 1922, 107, 487.

[5] Hammar, J. A., *Zeitsch. Anat. Entwickl.*, 1934, 193, 86.

[6] Thompson, P., *Jour. Anat.*, 1901, 35, 127; Paramore, R. H., see note [1], Elftman, H. O., *ibid.*, 1932, 51, 307 (pelvic floor in anthropoids). The account given in the text of this book is based on dissections made by the author while in Siam, 1889-1892.

[7] This sentence requires amplification. Dr. W. H. Lewis (*Anat. Rec.*, 1922, 23, 177) noted that the cells of a developing limb bud are in touch, not in continuity, with each other. The mesodermal cells within the ectodermal covering of the bud may be spoken of as mesenchyme (see p. 574), but it is better to reserve the latter term to designate developing cells which will become a vascular or reticular tissue. "Blastema" is used in much the same sense as "anlage"—meaning embryonic cells destined to become an organ, a system or some special structure.

on its surface; the fibres, with unchanged cytoplasm round their nuclei, have become enclosed in a special sheath—the sarcolemma. surrounding cells by their protoplasm assuming a striated appearance—the striae being confined to the periphery of the cell, the nucleus remaining central (Fig. 521, *A*). By the beginning of the 4th month myoblasts have become elongated; they are now multinucleated, the nuclei being arranged along the core of the cell—within the striated cortex [25]. A cell is thus transformed into a fibre as a result of repeated nuclear divisions being unattended by division of the cell body. Fibres retain an end to end union. At the beginning of the 5th month of development the embryonic fibres undergo a further radical change. The nuclei are no longer arranged along the core of the fibre, but have moved to a position on its surface; the fibres, with unchanged cytoplasm round their nuclei, have become enclosed in a special sheath—the sarcolemma.

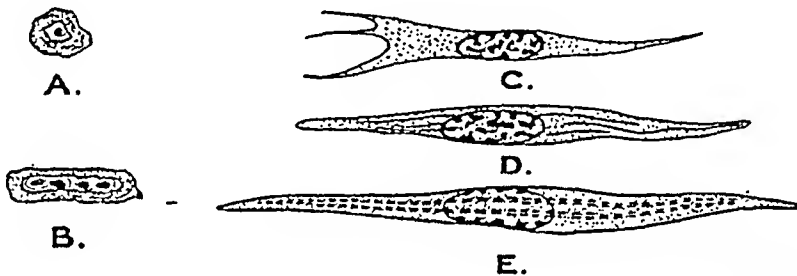


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R. W., *ibid.*, 1935, 69, 20 (on action of fibres); Carey, E. B., *Amer. Jour. Anat.*, 1936, 59, 89 (influence of tension on development); 1936, 58, 259 (striation).

[26] Bardeen, C. R., *Amer. Jour. Anat.*, 1907, 6, 259.

[27] Cuajunco, F., *Contrib. Emb.*, 1927, 19, 45; Tiegs, O. W., *Jour. Anat.*, 1932, 66, 300; Hewer, Evelyn E., *ibid.*, 1935, 69, 369.

[28] Carey, E. J., *Amer. Jour. Anat.*, 1921, 29, 341; *Jour. Morph.*, 1923, 37, 1, 37; *Radiology*, 1928, 10, 243; 1929, 33, 127.

[29] Haines, R. W., *Jour. Anat.*, 1932, 66, 578.

[8] For observation on the origin of connective tissue, ground substance, see Lewis, Mrs. M. R., *Contrib. Emb.*, 1922, 9, 121; Maximow, A., *Zeitsch. Mik. Anat. Forsch.*, 1929, 17, 625; Clark, E. and E., *Amer. Jour. Anat.*, 1940, 67, 255; Stearns, Mary L., *ibid.*, 1940, 67, 55; 1940, 66, 133; Iasswain, G., *Quart. Jour. Mic. Sc.*, 1935, 78, 271; Thurnesse, A., *Archiv. Biol.*, 1935, 46, 147.

[9] Parsons, F. G., *Jour. Anat.*, 1910, 44, 153.

[10] The development of the supra- and infra-umbilical parts of the body wall has been reinvestigated by Dr. G. M. Wyburn (*Jour. Anat.*, 1937, 71, 201; 1938, 72, 614; 1939, 73, 289).

[11] It is possible that the ventral sheet (represented by the rectus) arises not from the dorsal segmental myotomes but from the primitive mesoderm formed in the hinder end of the primitive streak. If this is so, then the segmentation of the rectus would be independent of the paraxial segmentation.

[12] For development of ribs, see Bardeen, C. R., *Amer. Jour. Anat.*, 1905, 4, 163; Mall, F. P., *ibid.*, 1906, 5, 433; Geddes, Auckland, *Jour. Anat.*, 1913, 47, 18; Harris, H. A., *Bone Growth in Health and Disease*, 1933.

[13] For ossification of sternum, see Botovansky, L., *Bull. Internat. l'Acad. tcheque Sc.*, 1931, 32, 309; Harris, H. A., *Jour. Anat.*, 1938, 72, 321 (absorption of fifth mesosternal segment).

[14] For number of ribs in primates, see Tredgold, A. F., *Jour. Anat.*, 1897, 31, 288; Schultze, A. H., *Amer. Jour. Physic. Anthropol.*, 1924, 7, 152; Cunningham, D. J., *Jour. Anat.*, 24, 127; Keith, Sir A., *ibid.*, 1903, 37, 8.

[15] Briscoe Sir Charlton, *Jour. Anat.*, 1925, 59, 432.

[16] Concerning the morphology of sternum, see Paterson, A. M., *The Human Sternum*, 1904; Whitehead and Waddell, *Amer. Jour. Anat.*, 1912, 12, 89.

[17] Cobb, W. M., *Jour. Anat.*, 1937, 71, 245 (supra-sternal ossifications).

[18] For development of sternum, see Frazer, J. E., *Manual of Embryology*, 1940; Gladstone and Wakeley, *Jour. Anat.*, 1932, 66, 508; Hanson, F. B., *Anat. Rec.*, 1920, 17, 1.

[19] Mueller, Charlotte, *Morph. Jahrb.*, 1906, 35, 591.

[20] Prof. Frazer (see note [18]) regards the manubrium as arising from both sternal bars, being bilateral in origin, each half being made up of two elements, one derived from the ventral end of the clavicle and the other of doubtful derivation.

[21] Keith, Sir A., *Jour. Anat.*, 1896, 30, 275; Hill's *Further Advances in Physiology*, 1909.

[22] Keith, Sir A., *Jour. Anat.*, 1896, 30, 275.

[23] Bardeen and Lewis, *Amer. Jour. Anat.*, 1901, 1, 145.

[24] Davies and Others, *Jour. Anat.*, 1932, 66, 323; Cave, A. J. E., *ibid.*, 1929, 63, 369 (distribution of 1st intercostal nerve); Walmsley, R., *ibid.*, 1937, 71, 404 (formation of sheath of rectus); Barlow, R. N., *Anat. Rec.*, 1934, 61, 413 (frequency and nature of sternalis).

[25] For development and innervation of muscle fibres, see Cuajunco, F., *Contrib. Emb.*, 1942, 30, 129; Speidel, C. C., *Amer. Jour. Anat.*, 1938, 62, 179 (repair of fibres); Katznelson, Z. S., *Anat. Rec.*, 1934, 61, 109; Glückmann, A., *Zeitsch. Anat. Entwickl.*, 1934, 103, 303; Lewis, W. H., *Contrib. Emb.*, 1926, 17, 1 (studied development of fibres of heart in cultural media); Lockhart and Brandt, *Jour. Anat.*, 1938, 72, 470; Gutmann and Young, *ibid.*, 1944, 78, 15 (repair of end plates); Gutmann, E., *ibid.*, 1945, 79, 1 (influence of nerve in preserving fibre); Clark and Blomfield, *ibid.*, 1945, 79, 15 (repair after devascularization); Haines,

anterior, preaxial or cephalic and posterior, postaxial or caudal. It is generally held that the lateral ridge, of which the limb buds are specialized parts, represents a continuous row of lateral fins. If this view is right, then the fore- and hind-limbs represent highly specialized fin-rays;

A section shows each bud to be composed of undifferentiated mesoderm, with a covering of ectoderm (Figs. 509, 529). The bud represents in structure a process of the undifferentiated mesoderm of the somatopleure or body wall; hence the limbs are to be regarded not as structures developed from the axis of the embryo, but as processes of the body wall.

At one time it was believed that extensions grow into each limb bud from the muscle-plate and skin-plate (dermatome) of the segments which are situated opposite the origin of the bud, but this view is not now

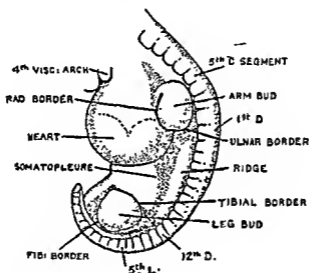


FIG. 522. Lateral view of a Human Embryo at the beginning of 5th week, showing the Limb-Buds, Lateral Ridges and Primitive Segments.

accepted [5]. Each corresponding segment of the spinal cord sends to the limb bud a nerve process. At least seven body segments contribute to the formation of each limb (Fig. 513). Outgrowths from the myotomes into the limbs have been observed only in the embryos of lower vertebrates; their occurrence in higher vertebrates was inferred. When the arm musculature becomes apparent as a mass in the 6th week, it shows no signs of separate segmental origin.

Experiments on Limb Buds.—Limb buds have been excised from tadpoles and developing chick embryos and kept alive by placing them in cultural media or transplanting them to other tadpoles or to the chorio-allantois of chick embryos. The results of such experiments go to prove that in limb buds, at their earliest stage, there is no "determination" of parts. Differentiation appears in the following order: first, the

CHAPTER XXIX

DEVELOPMENT AND DIFFERENTIATION OF THE LIMB BUDS

Evolution of Limbs.—The nature of the primitive structures from which limbs were evolved is still a much debated question [1]. The manner of their development in vertebrate embryos makes it certain that they were not outgrowths from the paravertebral or axial system; in every case they sprout out from the somatopleure, the outer wall of the body cavity, and are always supplied by the nerves of that lamina—the ventral branches of the spinal nerves [2]. We are also certain that the limbs correspond to the pectoral and pelvic fins of fishes. It is clear that when land-living vertebrates were evolved, the slight structures which were equal to the balancing and finer movements of an animal suspended in water had to undergo great modifications in order to become capable of moving and supporting the body on a solid medium. It was with the evolution of pulmoniferous land-living vertebrates that a very definite type of limb made its appearance. In all cases the limb of a primitive Tetrapod is built on the same plan; it is made up of a basal segment or girdle, with a free part divided into proximal, middle and distal segments. The distal segment carried 5 digits.

Although man has departed greatly from the primitive mammalian type in the structure of his brain and trunk, yet in the elements which enter into the formation of his limbs he has retained more of the ancestral mammalian features than many other mammals. He retains the original number of digits; the bones of his hand and foot are much less specialized than those of the horse. It is true that the skeleton of his lower extremity has been extensively modified for his plantigrade posture, yet under all the adaptational features one can see very clearly the outlines of a most primitive form. He comes of a stock which led an arboreal existence almost from the dawn of the mammalian type [3].

Embryonic Limbs.—The limbs begin to appear at the end of the 4th week [4]. A slight elevation or ridge is then seen to run along the dorsal border of the somatopleure, at some distance from the row of primitive segments formed in the paraxial mesoderm (Fig. 522). The limb buds spring from this ridge as flat processes with an upper, dorsal or extensor surface, and a lower, ventral or flexor surface; the arm bud is some two days in advance of the leg bud. The two borders are

the result of local arrests of the embryonic circulation [9]. Often fibrous bands are formed as a result of local necroses—such bands being erroneously regarded as of amniotic origin (see p. 71).

The *Internal Differentiation of Tissues* begins at the basal part of the limb and spreads towards the digits, the terminal phalanges being the



FIG 524 Four stages in the development of the Lower Limb—at the 5th, 6th, 7th and 8th weeks (After His)

last of the skeletal parts to become differentiated (8th week). The mesoderm forms the bud and forms the limb in the 6th week. The centres of chondrification are to be formed there occur first a condensation and then later, within the septal

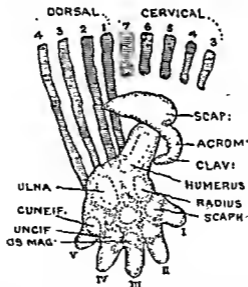


FIG 525 The Skeletal Blastema of the Upper Extremity of a Human Embryo in the 7th week of development. The centres of chondrification are indicated (W. H. Lewis)

condensation, an open formation in the arrangement of the cells. Centres of chondrification appear in the skeletal blastema of the arm late in the 6th week (shaft of humerus) and the leg in the 7th week (shaft of femur). The condition of the skeletal blastema of the arm of a human foetus in the 7th week of development is shown in Fig. 525. The centres of

preaxial border is determined ; secondly, the transverse axis, proximal and distal parts being thus determined ; thirdly, extensor (dorsal) and ventral (flexor) surfaces become fixed in their destiny. Thus the results obtained by transplantation will depend on the stage of differentiation reached by the transplanted bud [6]. The early experiments of Dr. Ross Harrison showed that the somatopleure can influence the development and characterization of undetermined limb buds [7]. If the limb bud of a tadpole is grafted in an inverted position—so that the extensor surface is applied to the somatopleure and the shoulder end directed ventrally—then such a bud suffers a transposition of parts ; if it was originally a right-arm bud it assumes the character of a left arm although implanted on the right side of the host tadpole. Limb buds may be evoked from the somatopleure by artificial stimuli ; the nasal placode when grafted on the side of a tadpole may cause the adjoining tissues to produce a limb bud [8]. The presence of nerves is not necessary for the full development of limb buds. On the other hand, if an extra limb bud is implanted, the posterior root ganglia which are dorsal to the graft increase in number and in size.

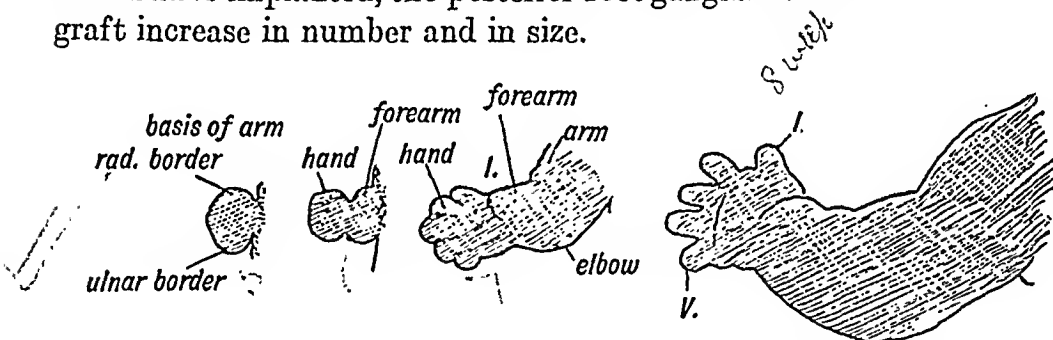


FIG. 523. Four stages in the development of the Upper Limb—at the 5th, 6th, 7th and 8th weeks. (After His.)

Changes in External Conformation.—In the 5th week (Fig. 523) the limb buds are unsegmented ; in the 6th a constriction marks the hand off ; the position of the elbow being indicated later in the same week. In the 7th week the fingers appear as thickenings in the *webbed* hand, the middle digit being indicated first. They become free at the end of the 8th week ; occasionally they remain attached, the child being born with its fingers in a *syndactylous* condition. The shoulder remains buried in the body wall ; the skeletal structures of the upper arm and thigh are the first to be differentiated ; those of the fore-arm and leg precede the cartilaginous differentiation of the shoulder and pelvic girdle. In all the embryological changes the upper extremity is some days ahead of the lower. Limb buds may undergo a complete arrest of growth and differentiation, appearing in the newly born child as mere papules. Or the limbs may undergo great damage and distortion as

of an adult were placed in the prone position, it would be necessary in order to restore the limbs to their embryonic position, (i) to draw them out at right angles to the axis of the body; (ii) to rotate the leg outwards so that the extensor surface of the knee is directed upwards, with the great toe in front and the little toe behind; (iii) the arm, on the other hand, would require to be rotated inwards to bring the elbow (extensor surface) into the dorsal position. The rotation which brings the embryonic limbs into the adult position appears to occur at the junction of the limb girdle with the trunk. If a limb bud is reimplanted in a rotated position, this rotation will become undone in the course of time, the tissues of the trunk bringing the bud back to its normal position [11].

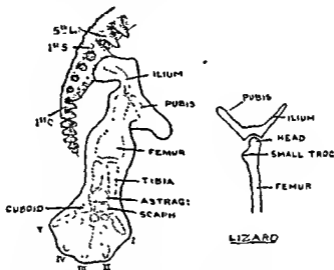


FIG. 526. The Skeletal Blastema of the Lower Extremity of a Human Embryo in the 7th week—14 mm long (Hardeen) Inset is the outline of the upper part of the Lower Extremity of a Lizard (Parsons)

Rotation of the Limb Girdle.—To estimate the extent of the rotation it is advantageous to compare the scapula and ilium and pick out their corresponding points. The extensors of the thigh and arm may be taken as guides [12]. The long head of the triceps and rectus femoris of the quadriceps manifestly correspond; their points of origin—the anterior border of the ilium and axillary border of the scapula—may be regarded as homologous points. The other corresponding points are shown in Fig. 527. The sacral articular surface of the ilium corresponds to part of the supra-spinous fossa. To restore the limb girdles to their primitive and corresponding positions, the scapula has to be rotated so that its axillary border comes to occupy the position normally held by the scapular spine, while the ilium has to be placed at right angles to the spine and its anterior border rotated outwards until it occupies a position

chondrification have appeared for the humerus, radius, ulna and certain of the carpal bones ; the centres for the phalanges have not yet begun. The scapula, acromion and clavicle (outer part) are continuous in the fibrous stage ; a common centre appears for scapula and acromion, the outer clavicular blastema is chondrified separately. Before the end of the 2nd month the cartilaginous bases of all the arm bones have appeared. Centres of ossification begin to form in the latter part of the 2nd month, and correspond generally to the centres of chondrification. During the 3rd month the skeletal blastema between the chondrified bases of the bones, by a process of vacuolation within and between the cells, opens out into a cavity and forms the synovial membranes of the joints (Fig. 551). By the end of the 6th week the proximal muscles, vessels and nerves are appearing ; a week later, they are also apparent in the distal parts of the limbs. The tissue left over, not included in these structures, forms their sheaths and the fasciae and connective tissue of the limb (see p. 573). The processes of nerve cells to form nerves and of the blastema to form muscle-fibres are apparent within the limb bud in the 6th week. The blood-vessels appear first as a capillary plexus which permeates the whole bud ; gradually the arterial stream becomes concentrated in one capillary chain which is established as the main artery of the bud. The blood from the capillary plexus passes to collecting marginal vessels, arranged along both anterior and posterior borders of the limb bud [10]. This plexus follows the ingrowing nerves ; in some mammals (the lemur, etc.) the embryonic plexus persists round nerves and forms the *plexus mirabilis*. The limb vessels are derived from the segmental branches of the aorta.

Skeletal Blastema of Lower Extremity.—About the end of the 7th week the blastema of the ilium becomes joined to the costal masses of the 1st, 2nd and 3rd sacral vertebrae (Fig. 526). The scapula, which at the beginning of the 2nd month lies opposite the 4th, 5th, 6th, 7th cervical vertebrae, retains its freedom (Fig. 525). By the end of the 7th week the cartilage centres have appeared for the majority of the bones of the lower extremity (Fig. 526). The centres for some of the tarsal bones and for the phalanges are formed before the end of the 2nd month, the terminal phalanges being demarcated before the middle phalanges and also ossified before them (Todd). The acetabulum develops at the site of union of the iliac, ischial and pubic cartilages at the end of the 2nd month. At that time the femur has no neck—a condition seen in reptiles (Fig. 526). The neck begins to form early in the 3rd month. In the 3rd month the symphysis pubis is formed.

Torsion and Rotation of the Limbs.—In the earliest stages the limb buds are so placed that the knee and elbow are directed upwards. If the body

senting a "mirror-image" of the right scapula—which certainly is true. Prof. M. R. Drennan, recognizing this truth, compares the left arm with the right leg and *vice versa* [15]. There is no evidence that a rotation of the elements of the limb girdles takes place during development. A reference to Fig. 528 will show that there is a correspondence between the structures on the postaxial border of the fore-limb and on the preaxial border of the hind-limb. The subscapularis, teres major and latissimus dorsi (*A*), derivatives of a common flexor mass, correspond to the ilio-psoas—also the derivative of a common flexor mass (*A*¹). The triceps and quadriceps (*C*, *C*¹) also agree; so do the olecranon and ulna with the patella and tibia. The specialization of the proximal digit of the hand to form a pollex and of the first of the foot to form a hallux occurs only in primates. The mirror-image theory particularly applies to the distribution of nerves. To explain this peculiar relationship which exists between the fore- and hind-limbs of the same side in vertebrates one is tempted to suppose that they represent anterior and posterior halves of a single primitive locomotory appendage; the line of separation is represented by the adjacent borders of the limbs. On such a theory the adjacent borders should be constituted alike.

Segmental Nature of the Limbs.—The nerves of the limbs, possibly also the muscles, vessels and skin, are derived from a number of the primitive body segments. The 4th cervical to the 2nd dorsal contribute to the formation of the upper extremity; the 1st lumbar to the 3rd sacral to the lower, but in man the extent to which the most anterior and most posterior of each of these contributes to the limb varies considerably. Since the processes of the skin- and muscle-plates of these segments retain in the limbs (so we infer from the study of limbs of lower vertebrates) their original nerve supply, it is evident that the muscles and skin of the human limbs may be assigned to their original body segments by a study of the distribution of the nerves. Such a study has been carried out by a great number of anatomists [16]. The primitive simple arrangement of muscle segments may be seen in the fins of certain fishes, but in man these segments have undergone much redivision and reassortment in the course of evolution; yet the primitive arrangement can be recognized.

Nerve Supply of the Limbs. *The Arm.*—It is important to note that the limb buds arise from the ventro-lateral aspect of the trunk (Fig. 529) near the junction of the somatopleure with the paraxial mesoderm. Therefore the nerves of the limbs are the nerves of the ventro-lateral zone [17]—the lateral cutaneous branches of the typical segmental nerves (Fig. 530). The muscles are derived from the ventro-lateral sheet, which gives rise to all the muscles of the body wall. As soon as the limb

corresponding to the axillary border of the scapula (see Fig. 527). The free edge of the spine (scapular) represents a former border of the scapula; the supra-spinous blade of the scapula appears first in mammals.

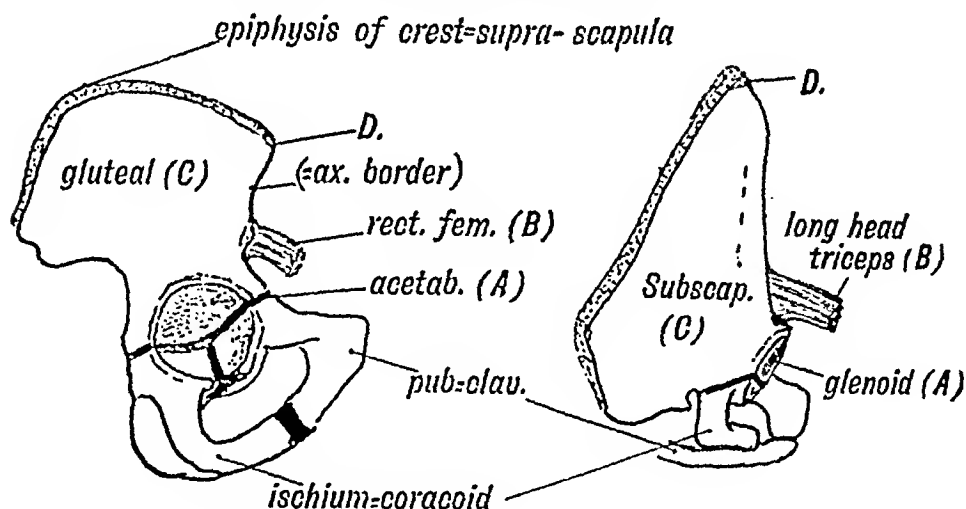


FIG. 527. The Corresponding Points (A, B, C and D) in the Ilium and Scapula.

There is manifestly a spiral twist in the humerus, but it is doubtful if this be in any way due to the torsion which the limb undergoes [11].

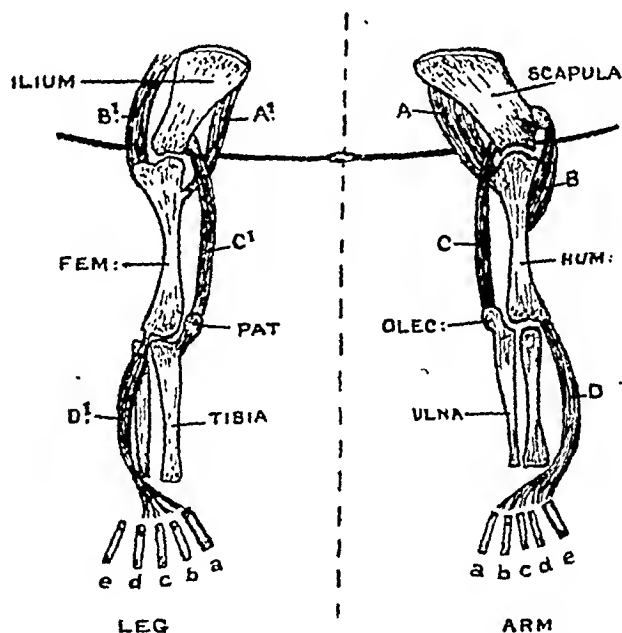


FIG. 528. Diagram of the Fore- and Hind-Limbs of the same side to show the "Mirror-image" Relationship between their Constituent Parts. The vertical line passing through the umbilicus is regarded as the centre from which the two limbs have become differentiated. (After Parsons and Geddes.)

Prof. Parsons [13] and Lord Geddes [14] have shown that although there is a direct correspondence in the elements of the upper and lower extremity, the correspondence is a reversed one—the right ilium repre-

plexus (Figs. 531, 532). As they enter the bud, the nerves encounter the condensed skeletal blastema at its base and divide into a dorsal or extensor set and a ventral or flexor set (Figs. 529, 530).

The relationship of the segmental nerves to the arm-bud in the 6th week of development is shown in Fig. 531—a drawing taken from Dr. George Streeter's research [18]. The base of the arm is then situated in the cervical region; the hypoglossal nerve issues almost at its anterior border. The arm descends tailwards during the 2nd month, the nerves consequently undergoing an elongation. The ventral divisions of the spinal nerves from the Vth cervical to the 1st dorsal have entered the bud, and already the chief nerves can be traced. The brachial plexus is formed; the interlacing of fibres does not arise owing to a compression of the nerves due to a lack of room, but represents a physiological or functional adaptation. Prof. Goodrich [19] found that in fishes only

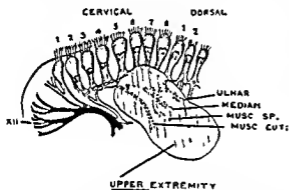


FIG. 531.

FIG. 531. The Arm-Bud and its Nerves in a Human Embryo in the 6th week of development (After Streeter.)

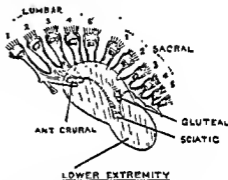


FIG. 532.

FIG. 532. The Bud of the Lower Extremity with its Relationship to Spinal Nerves in a Human Embryo in the 6th week of development. (After Streeter.)

the posterior root or sensory fibres entered into the plexiform arrangement—the motor or ventral fibres proceed into the limb without exchanging fibres. By the beginning of the 3rd month all the muscles and nerves are differentiated. In Fig. 530 the distinction between the nerves of the extensor and flexor aspects of the limb is shown.

In Fig. 532 the bud of the hind-limb of the same embryo is represented. It will be seen that the stage of development is less advanced than in the arm. The crescentic base of the limb is in relationship with the spinal nerves from the 1st lumbar to the 3rd sacral. The crural and sciatic plexuses are continuous; their separation occurs in the 7th week, when the ilium becomes attached to the costal processes of the first three sacral vertebrae.

The nerve supply assists to indicate the body segments in connection

buds appear, bundles of fibres from the anterior and posterior nerve roots of the corresponding body segments enter them and keep time with their

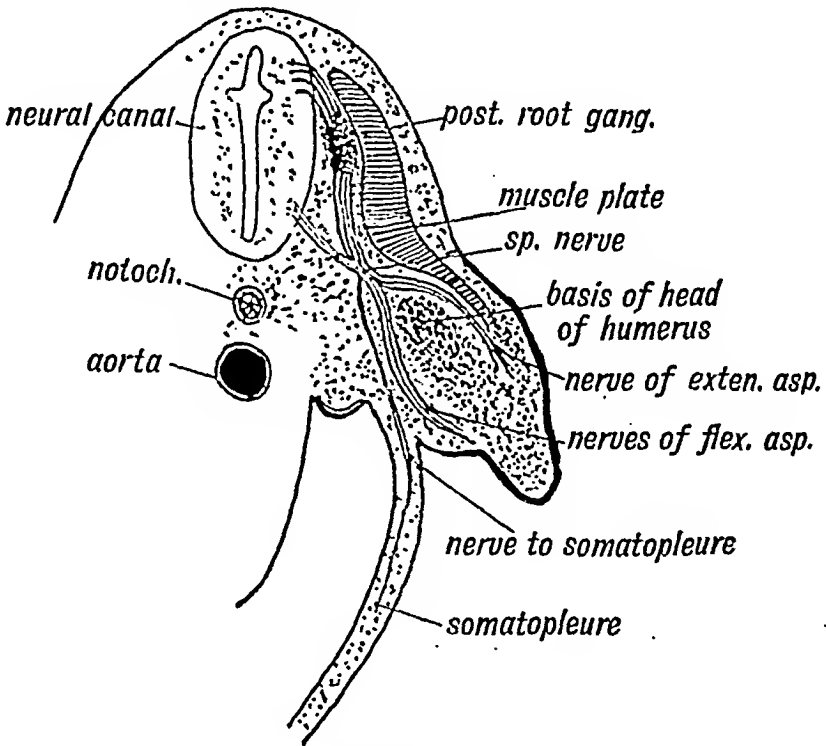


FIG. 529. Section of the Arm Bud of a Human Embryo at the end of the 5th week. (Alex. Low.)

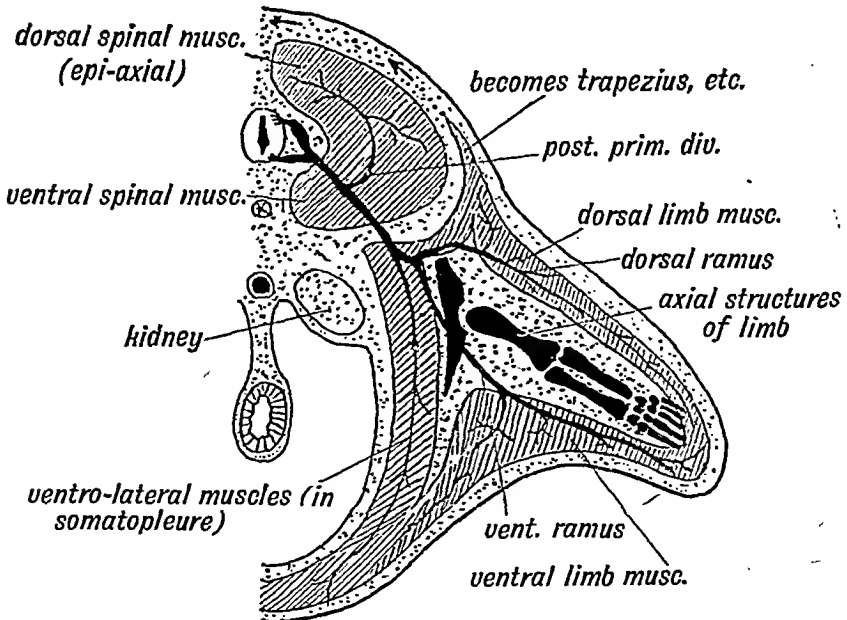


FIG. 530. Schematic section to show the primitive grouping of the Nerves and Musculature of Limbs. (After Kollmann.)

growth. The limb nerves are at first so large in comparison with the size of the limb bud that they are crowded together and already form a

joins the median below the insertion of the coraco-brachialis; this communication is very common in lower primates; its meaning is not known. (iii) A communication between median and ulnar in the forearm is also common and is seen constantly in some primates. The communicating branch passes with the deep branch of the ulnar nerve to the palm. It is also manifest that there is a correspondence between the musculo-spiral (radial) nerve on the proximal border of the arm and the sciatic on the distal border of the leg.

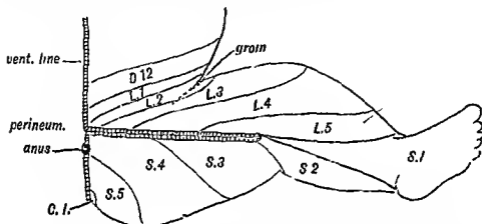


FIG 534 Diagram to show the typical manner in which the Posterior Nerve Roots are distributed in the Lower Limb (based on Sherrington's researches into the Sensory Distribution of the Limb Nerves of Apes)

Formation of Nerve Plexuses depends on the following factors [22]:

(i) Each skin segment is supplied not only by its own nerve but by the nerve of the segment in front of it and behind it. (ii) A muscle segment, such as may be seen in the rectus abdominis, is supplied by its own and the two adjacent nerves, the fibres forming a plexus before entering the muscle. (iii) Each muscle is formed by the combination of parts of two or more segments, and therefore its nerve rises from two or more spinal nerves. (iv) The muscles of the limbs have migrated from their original positions and carried their nerves with them. (v) Most important of all, the afferent or sensory fibres from a muscle have to be linked to the spinal centres of all its antagonists or coadjutors. These are some of the circumstances which have led to nerve fibres being assorted into definite cords at their first outgrowth.

Nerve Supply of the Lower Limb.—Usually ten segments contribute to the nerve supply of the lower limb—the 12th dorsal to the 4th sacral (Fig. 535). The sensory nerves are derived from these segments; the motor nerves begin at the 1st lumbar segment and end at the 3rd sacral. There is a considerable variation in the number of body segments or vertebrae to which the lower limb is attached; usually it is the 25th vertebrae that becomes the 1st sacral, but it may be the 26th or 24th

with which the arm is developed (Fig. 533). The 4th cervical is the most anterior; the 2nd dorsal, sometimes it is the 3rd, is the most posterior segment. Hence the arm is produced from seven, or more commonly eight, segments in all. Each segment contributes from its nerve, its muscle-plate and probably also, at a very early stage of development, from its artery [20]. The typical distribution of a segmental nerve to

the limb-bud is shown diagrammatically in Fig. 530. Each segmental nerve, as is the case with the typical lateral cutaneous nerves, divides into a *dorsal* division for the extensor muscles and *ventral* for the flexor muscles. The nerves to the extensor muscles form the dorsal divisions and cord of the brachial plexus; the nerves to the flexor muscles form the ventral divisions and the outer and inner cords. The processes to the limbs from the skin-plates and muscle-plates are also divided into dorsal and ventral sets: the one set making up the extensor aspect of the limb, the other the flexor aspect.

Clinical and experimental research have shown that each of the seven or eight segments contributes to the cutaneous supply of the limb. The classical investigations of Sherrington [21] into the segmental distribution of the sensory nerves in the limbs of apes showed that they are arranged in a definite and orderly manner (Fig. 534). The sensory distribution of the spinal nerves in the human arm is shown diagrammatically in Fig. 533. The

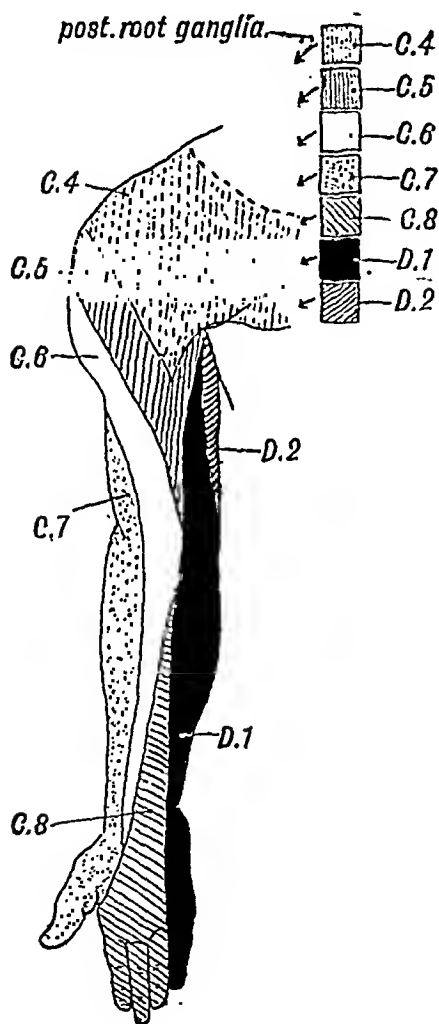


FIG. 533. The Distribution of the Posterior Roots of the Spinal Nerves on the Flexor Aspect of the Arm.

distribution of the motor nerves of each segment is fully described in anatomical text-books.

Only three anomalous points in the arrangement of nerves in the upper limb require attention: (i) The segments which supply nerves for the arm are nearly constant. The extent to which the 4th cervical and 3rd dorsal contribute varies; the degree of variation is markedly less than in the lower limb. (ii) A part of the musculo-cutaneous nerve often

joins the median below the insertion of the coraco-brachialis; this communication is very common in lower primates; its meaning is not known. (iii) A communication between median and ulnar in the forearm is also common and is seen constantly in some primates. The communicating branch passes with the deep branch of the ulnar nerve to the palm. It is also manifest that there is a correspondence between the musculo-spiral (radial) nerve on the proximal border of the arm and the sciatic on the distal border of the leg.

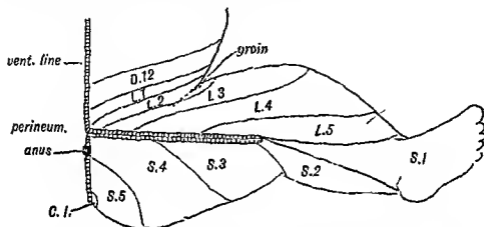


FIG 534. Diagram to show the typical manner in which the Posterior Nerve Roots are distributed in the Lower Limb (based on Sherrington's researches into the Sensory Distribution of the Limb Nerves of Apes)

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(p. 89). Of these three forms, the first is the normal type (25th); the second the post-fixed type (26th); the third the prefixed type (24th). There is even a greater variation in the segments which contribute nerves to the limb; the *normal* motor segments are the 1st lumbar to the 3rd sacral; in the *post-*

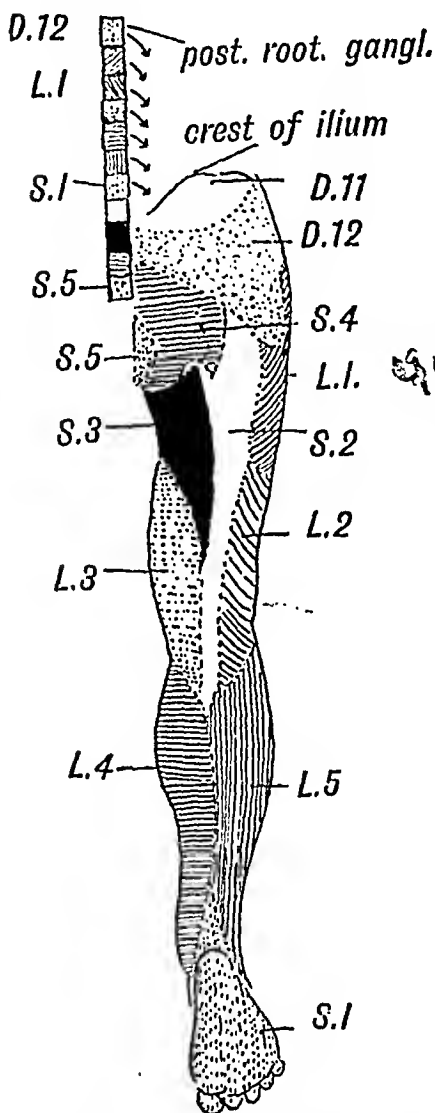


FIG. 535. Flexor aspect of the Lower Limb, showing the Sensory Distribution of the Segmental or Spinal Nerves.

fixed type (a more common type than the next) the motor segments commence at the 2nd lumbar and cease at the 4th sacral; in the *pre-fixed type* the motor segments commence at the 12th dorsal and end at the 2nd sacral. These three types grade into each other. The spinal nerve which bifurcates and joins both lumbar and sacral plexuses is known as the *nervus furcalis*. In the normal type it is the IVth lumbar; in the pre-fixed type it is the IIIrd lumbar; in the post-fixed type the Vth lumbar. The *nervus bigeminus*, going to sacral and pudendal plexuses and which is normally the IIIrd sacral, may also vary in a corresponding manner.

The nerves to the extensor surface of the lower limb, the anterior crural (femoral), external popliteal (common peroneal), etc., represent the *dorsal divisions* of lateral cutaneous nerves (Fig. 530). The nerves to the adductor and flexor aspects, the obturator and internal popliteal (tibial), represent the *ventral divisions*. In a considerable number of individuals the dorsal division (external popliteal) and ventral (internal popliteal) of the great sciatic separate in the pelvis, the external popliteal per-

forating the pyriformis. The segmental distribution of the motor nerves in the lower extremities is given at length in text-books on anatomy. The muscular segments correspond approximately in their distribution with those of the skin. It will be remembered that the perineal region is developed behind the limb buds of the lower extremities (Fig. 513): hence its nerve supply from the most posterior nerve segments (3rd and 4th sacral).

Sherrington found that the posterior roots of the limb nerves were distributed in a regular and simple manner in apes. His results are applied to the lower limb of a human foetus in Fig. 534. The actual distribution in man, which has not been completely worked out by clinicians, varies considerably from what might be expected from Sherrington's results (compare Figs. 534 and 535).

In the human leg and foot there is a tendency for nerve fibres destined for the outer digits to proceed in the external saphenous (sural) nerve instead of by the musculo-cutaneous (superficial peroneal). The external saphenous nerve may supply the 4th and 5th digits (the ancestral form) in a manner similar to the ulnar nerve in the hand; more frequently it is confined to the outer side of the 5th digit. The outgrowing fibres of the obturator nerve may be divided into ventral and dorsal parts by the blastema of the pubis. In such a case the more ventral fibres cross the ramus of the pubis and form the *accessory obturator* nerve.

How do nerve fibres which enter a developing limb bud find their way to their appropriate destinations? There is some mode of guidance, but its nature remains uncertain. If the entrance of nerve fibres from one or more segments is prevented, their place is taken by fibres from adjoining segments. If a muscle is deprived of its innervation, it manifests a power of attracting a fresh supply [23].

Vessels of the Limbs.—When the limb buds are being formed in the 5th week they are permeated by a capillary network, which in the case of the arm is chiefly fed by the artery of the 7th cervical segment [24], while in the case of the leg-bud the chief axial artery arises from a pelvic arterial plexus—soon connected with the internal iliac (hypogastric) artery. During the 6th week the main arteries of the limbs are being evolved from pathways in the primary capillary plexuses; by the end of the 8th week, all the important arterial channels have been laid down. Every student knows how frequently the arteries of the leg and arm depart from the arrangement which is regarded as normal. Comparative anatomy and embryology throw light on these arterial anomalies [25].

In Figs. 536, 537, the upper and lower limbs have been placed in corresponding positions—the extensor surfaces being directed upwards and a scheme of their arteries depicted in relationship to their skeletal elements. In each limb bud there is developed a main or axial artery, certain parts of which are suppressed in the 8th week while other accessory vessels are developed. The axial artery of the upper limb persists as the subclavian, axillary and brachial trunks, but in the lower limb the corresponding trunk (Fig. 537) is suppressed, as Prof. Senior has shown, during the 8th week of development—save for the sciatic branch of the internal iliac artery and the anastomotic chain along the sciatic

investigations, the axial artery passes deep to the popliteus muscle; the part which lies deep to the muscle becomes reduced during the 8th week and a new vessel develops superficial to the muscle. The part of the popliteal artery proximal to the popliteus muscle is derived from the axial vessel, the part lying on the popliteus from the new trunk. In the antecubital space the corresponding axial vessel disappears, the terminal part of the brachial artery with its divisional trunks—the ulnar and radial arteries—representing later channels.

In the fore-arm the axial vessel is represented by the anterior (volar) interosseus, continued into the hand to give off the palmar interosseus vessels—the primary blood supply of the hand. On the extensor or dorsal aspect of the interosseus membrane of the fore-arm develops the dorsal interosseus artery of the fore-arm fed by branches of the axial artery which perforate at the proximal and distal ends of the membrane (Fig. 536). In the leg the axial artery disappears, save its distal part, which is incorporated in the peroneal artery (Fig. 537). As in the fore-arm, perforating branches pass to the dorsal aspect of the interosseus membrane to form the anterior tibial artery.

Having thus traced the fate of the axial artery in each limb, we now turn to the origin of the great secondary channels. The external iliac artery and its continuation, the femoral artery, open up a new channel to the lower limb along the course of the anterior crural or femoral nerve. The channel arises from the umbilical artery proximal to the origin of the internal iliac (the axial vessel), and by the end of the 7th week has effected a union with that part of the axial vessel which lies in the popliteal space (Fig. 537). In the upper limb there is no corresponding arterial trunk, although communications between the suprascapular (transverse scapular), circumflex and superior deep branch of the brachial artery may represent it. In both the leg and fore-arm more superficial secondary channels are formed—the ulnar and posterior tibial arteries and their branches which end in the superficial palmar and plantar arches (Figs. 536, 537). In all primates with the exception of man, the femoral artery, before piercing the adductor magnus, gives off a large branch, the *saphenous artery*, which accompanies the long saphenous nerve and turns to the extensor aspect of the leg above the internal malleolus, where it becomes the dorsal artery of the foot [25, Aaser]. At no stage of human development does the saphenous artery serve as a main channel, but the superficial branch of the *anastomotica magna*, which represents this vessel in man, is more highly developed at the 8th week than it is at any subsequent period. The saphenous artery corresponds to the radial of the upper limb.

Vas Aberrans.—At a very early stage (7th week) there is developed

nerve which links together branches of the sciatic and popliteal arteries. On the flexor aspect of the elbow, as in the corresponding space—the

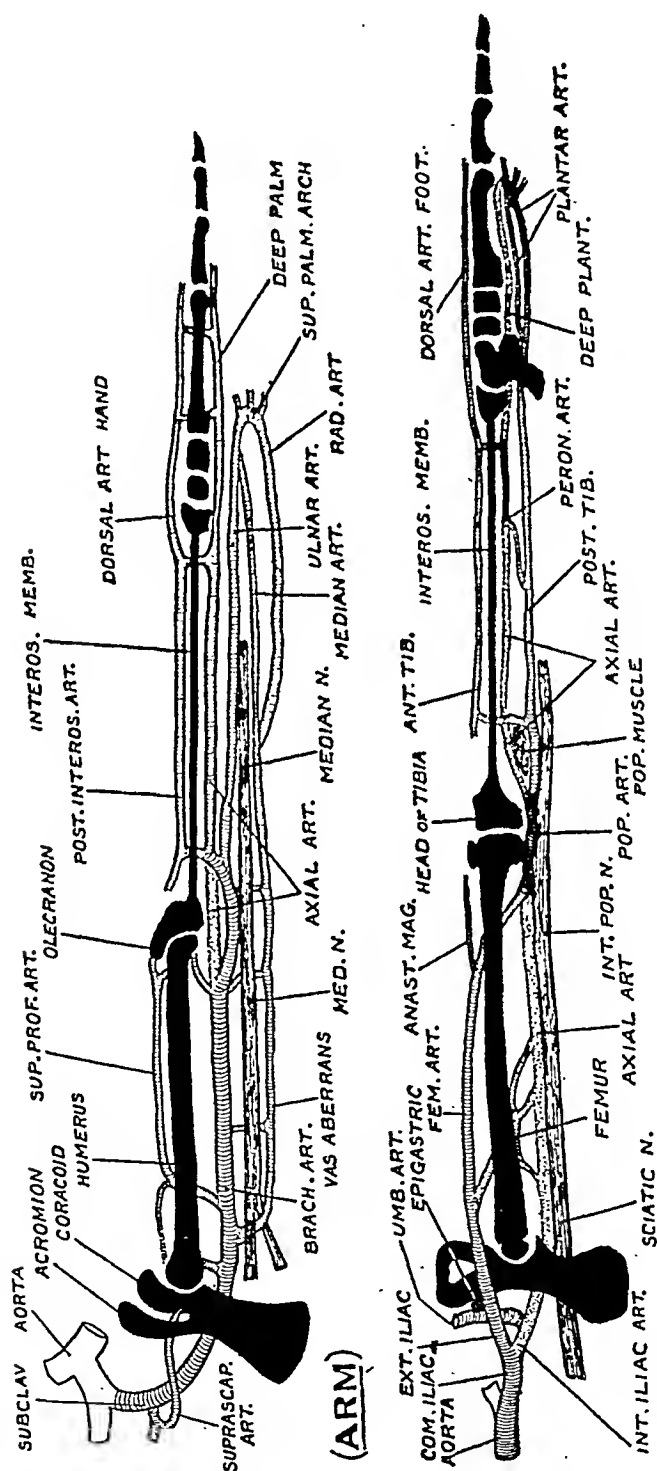


FIG. 536. Scheme of Arteries of the Upper Extremity—the limb being placed with its flexor surface downwards so as to be comparable to Fig. 537.

FIG. 537. Scheme of Arteries of the Lower Extremity. The parts of the axial vessel which are stippled become obliterated.

popliteal—of the lower limb, the axial artery undergoes a degree of suppression. In the popliteal space, as we know from Prof. Senior's

investigations, the axial artery passes deep to the popliteus muscle; the part which lies deep to the muscle becomes reduced during the 8th week and a new vessel develops superficial to the muscle. The part of the popliteal artery proximal to the popliteus muscle is derived from the axial vessel, the part lying on the popliteus from the new trunk. In the antieubital space the corresponding axial vessel disappears, the terminal part of the brachial artery with its divisional trunks—the ulnar and radial arteries—representing later channels.

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Vas Aberrans.—At a very early stage (7th week) there is developed

along the superficial aspect of the median nerve an arterial anastomotic channel fed by a succession of branches which spring from the axial brachial vessel (Fig. 536). This channel frequently opens up in part or even in its whole extent and gives rise to the greater number of arterial anomalies met with in the arm. The *vas aberrans* may replace the main artery, being known from the normal brachial artery by the fact that it lies superficial to the median nerve, whereas the usual vessel is deep to that nerve. The first ramus of the *vas* appears between the heads of the median nerve (Fig. 536). The ulnar or radial artery frequently arises from the brachial artery in the lower third of the arm; in such cases the upper part of the radial or ulnar vessels will be found to be formed out of the anastomotic channel. In the fore-arm the median artery may be of large size, ending in the superficial palmar arch; it too is formed out of the arterial anastomosis which is laid down in foetal life, superficial to the median nerve.

Superficial Veins.—During the 6th week the terminal margin of the limb buds is fringed with a venous plexus which becomes broken up by the outgrowth and differentiation of the digits [26]. The terminal plexus is drained by a vein which passes upwards on the ulnar or peroneal margin of the limb, this marginal vessel becoming the superficial ulnar and basilic veins in the arm and the external saphenous vein in the leg. Later, radial and tibial marginal venous channels are formed, becoming the radial and cephalic veins in the upper limb and the long or internal saphenous in the lower. The cephalic vein originally crossed the clavicle and terminated in the external jugular vein, as is the rule in apes, but later ended in the axillary vein, below the clavicle. In man only does the long saphenous vein terminate in the groin by piercing a hiatus in the fascia lata; in all other primates it ends above the internal (medial) condyle of the femur by joining the femoral veins in Hunter's canal.

Malformation of the Limbs.—As already mentioned (p. 73), the limb buds may be arrested at a very early stage of development or they may undergo various degrees of deformity as a result of *plastic necrosis*. This disorder, with its attendant malformations, has been produced in young rats by Dr. H. J. Bagg by exposing parent rats to X-rays [9]. Dr. Streeter has described corresponding lesions in human fetuses [9]. If an arrest in the backward segmentation of the trunk should occur before the sacral region is reached, then the right and left leg-buds become fused and the condition known as *sympodia* is produced [28]. The digits of both limbs are liable to a great number of malformations—such as non-separation (*syndactyly*) and imperfect delimitation of the middle phalanx (*brachydactyly*) [29]. The radius may be absent in the arm and the tibia in the leg [30]. When the radius is absent the thumb also is

usually missing. Extra digits may be present—most usually on the radial side of the thumb or on the ulnar side of the little finger [31]. A digit may be imperfectly cleft; so too the foot—less frequently the hand.

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- [3] Wood-Jones, F., see note [1].
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- [9] Bagg, H. J., *Amer. Jour. Anat.*, 1929, 43, 167 (production of hereditary malformation of limbs). See also note [26], Chapter IV.
- [10] Woollard, H. H., *Contrib. Emb.*, 1922, 14, 137.
- [11] Nicholas, J., *Jour. Exper. Zool.*, 1924, 40, 113; Evans and Krahle, *Amer. Jour. Anat.*, 1945, 76, 503 (torsion of humerus).
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[23] See Weiss, Paul, *Jour. Comp. Neur.*, 1937, 66, 181; Nicholas, J. S., *ibid.*, 1933, 57, 253.

[24] Woollard, H. H., see note [10].

[25] For development of vessels of limbs, see Senior, H. D., *Jour. Anat.*, 1919, 53, 131; *Amer. Jour. Anat.*, 1919, 25, 55; 1924, 33, 243; 1925, 36, 1; Muller, E., *Anat. Hefte*, 1903, 22, 377; Woollard and Weddell, *Jour. Anat.*, 1935, 69, 25 (peripheral anastomosis); Schwyzer and De Garis, *Anat. Rec.*, 1935, 63, 405 (forms of superficial brachial artery). Comparative anatomy of vessels of limbs in primates: Manners-Smith, *Jour. Anat.*, 1910, 44; 1911, 45; 1912, 46; Kosinski, C., *Jour. Anat.*, 1926, 60, 140, 274; Aasar, Y. H., *ibid.*, 1939, 73, 194 (internal saphenous artery in man).

[26] See under note [10].

[27] Bagg, H. J., see note [9].

[28] Johnston, T. B., *Jour. Anat.*, 1920, 54, 208; Boulgakow, B., *ibid.*, 192, 63, 255; Fraedrich, G., *Ueber die menschlichen Sireniform Missbildungen*, 1938.

[29] For accounts of malformation of limbs, see notes [9], [26], Chapter IV; also Bell, Julia, *Ann. Eug.*, 1930, 4, 41; *ibid.*, 1931, 4, 233; Barge, J. A., *Zeitsch. Anat. Entwick.*, 1930, 93, 253; Pires de Lima, J. A., *As anomalias dos membros nos Portugueses*, Porto, 1927; *Jour. Anat.*, 1928, 62, 333; Drinkwater, H., *ibid.*, 1916, 50, 178; Shore, L. R., *ibid.*, 1926, 60, 420; Sverdrup, A., *Jour. Genetics*, 1923, 15, 217; Colwell, H. A., *Jour. Anat.*, 1928, 62, 183; Cooperman, M. B., *Jour. Bone. Joint. Surg.*, 1930, 12, 956; Cockayne, F. A., *Jour. Anat.*, 1933, 67, 166.

[30] Smith, Ross, *Jour. Anat.*, 1928, 62, 238; Dankmeyer, J., *Anat. Rec.*, 1935, 62, 179; Wakeley, C. P. G., *Jour. Anat.*, 1931, 65, 506.

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CHAPTER XXX

MORPHOLOGY OF THE LIMBS

In the previous chapter the chief events connected with the development of the limb buds in the human embryo have been noted and incidentally certain points relating to the morphology—primitive structure—of the limbs have been alluded to. In the present chapter we propose to deal with the more important problems relating to the pectoral and pelvic girdles, to the bones of the hand and foot and to the significance of certain muscular modifications.

Congenital Elevation of the Shoulder.—We have already seen that the arm of the human embryo is cervical in position,—in this respect

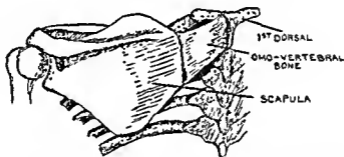


FIG 538. The Omo-vertebral Bone in a Case of Congenital Elevation of the Shoulder.

resembling the pectoral fins of fishes. It descends during the 2nd month, reaching its final position over the ribs in the 3rd month. Its descent is accompanied not only by an elongation of the brachial nerves but also by a downward migration of certain muscles—originally placed in the neck—trapezius, serratus magnus, latissimus dorsi and pectoral muscles. The descent may be arrested. Such an arrest, which is not rare in children, is often accompanied by irregularities in the formation of the cervical vertebrae—for the elongation of the cervical region to form a neck is related to the descent of the shoulder, of the heart and of the diaphragm—and with the appearance of a skeletal element of the shoulder girdle which is present in certain fishes (dipnoi and selachians). This omo-vertebral element is represented in Fig. 538—from the classical case of Willet and Walsham (1880). In fishes this bone joins the suprascapula to the occiput; when it appears in man it is usually fixed to or articulates with the spinous processes of the lower cervical vertebrae [1].

[22] Harris, Wilfred, *The Brachial Plexus*, 1939; Braus, A., *Verhand. Anat. Gesellsch.*, 1910, p. 14.

[23] See Weiss, Paul, *Jour. Comp. Neur.*, 1937, 66, 181; Nicholas, J. S., *ibid.*, 1933, 57, 253.

[24] Woollard, H. H., see note [10].

[25] For development of vessels of limbs, see Senior, H. D., *Jour. Anat.*, 1919, 53, 131; *Amer. Jour. Anat.*, 1919, 25, 55; 1924, 33, 243; 1925, 36, 1; Muller, E., *Anat. Hefte*, 1903, 22, 377; Woollard and Weddell, *Jour. Anat.*, 1935, 69, 25 (peripheral anastomosis); Schwyzer and De Garis, *Anat. Rec.*, 1935, 63, 405 (forms of superficial brachial artery). Comparative anatomy of vessels of limbs in primates: Manners-Smith, *Jour. Anat.*, 1910, 44; 1911, 45; 1912, 46; Kosinski, C., *Jour. Anat.*, 1926, 60, 140, 274; Aasar, Y. H., *ibid.*, 1939, 73, 194 (internal saphenous artery in man).

[26] See under note [10].

[27] Bagg, H. J., see note [9].

[28] Johnston, T. B., *Jour. Anat.*, 1920, 54, 208; Boulgakow, B., *ibid.*, 192, 63, 255; Fraedrich, G., *Ueber die menschlichen Sireniform Missbildungen*, 1938.

[29] For accounts of malformation of limbs, see notes [9], [26], Chapter IV; also Bell, Julia, *Ann. Eug.*, 1930, 4, 41; *ibid.*, 1931, 4, 233; Barge, J. A., *Zeitsch. Anat. Entwickl.*, 1930, 93, 253; Pires de Lima, J. A., *As anomalias dos membros nos Portugueses*, Porto, 1927; *Jour. Anat.*, 1928, 62, 333; Drinkwater, H., *ibid.*, 1916, 50, 178; Shore, L. R., *ibid.*, 1926, 60, 420; Sverdrup, A., *Jour. Genetics*, 1923, 15, 217; Colwell, H. A., *Jour. Anat.*, 1928, 62, 183; Cooperman, M. B., *Jour. Bone. Joint. Surg.*, 1930, 12, 956; Cockayne, F. A., *Jour. Anat.*, 1933, 67, 166.

[30] Smith, Ross, *Jour. Anat.*, 1928, 62, 238; Dankmeyer, J., *Anat. Rec.*, 1935, 62, 179; Wakeley, C. P. G., *Jour. Anat.*, 1931, 65, 506.

[31] Lineback, P. E., *Anat. Rec.*, 1921, 21, 313; Smith and Boulgakow, *Jour. Anat.*, 1924, 58, 359 (a separated hallux).

portion of the mesenchymal arch are developed two cartilaginous elements, the *pubis* and *ischium*, both of which take part in the formation of the acetabulum (Fig. 539). Both reach the ventral median line in which a median bar of cartilage is developed (see Fig. 516, B).

In man the following changes may be noted : (i) The costal processes of the sacral vertebrae ($2\frac{1}{2}$ usually) have fused together to form the lateral sacral mass ; with these the ilium articulates (Fig. 526) ; (ii) the vertebral border (crest) has become enormously elongated and gives attachment to abdominal muscles, cutting off the fibres of insertion of the external oblique which form the chief part of Poupart's ligament ; (iii) the ischium does not reach the ventral line. Up to the 4th month of development the bond between the ilium and sacrum is fibrocartilaginous in nature. In this bond there then are formed several synovial spaces, which subsequently fuse to form the synovial lining of the sacro-iliac joint [3]. The ligaments of the sacro-iliac joints, and particularly those of the symphysis, are sensitive to the action of oestrogens and undergo relaxation in the terminal months of pregnancy. This is especially true of animals which bear large-sized young, such as guinea-pigs [4]. The human ilium may effect contact not only with the costal elements of the sacrum but also with those which represent transverso processes [5].

In most birds neither ischium nor pubis reaches the ventral line. The pubes fail to meet in cases of *ectopia vesicae*, just as the sternum is cleft in cases of *ectopia cordis*. The symphysis pubis is formed in the ventral line during the 3rd month [6]. The cotyloid bone—or acetabuli—is formed in the Y-shaped cartilago between the three elements. It ossifies in the 13th year [7]. This ossification forms the pubic part of the acetabulum, and is really part of the pubis.

The median pelvic bar corresponds to the sternum and like it is of bilateral origin. In reptiles (Fig. 516) it is divided into anterior, middle and posterior parts. The anterior parts, which represent the marsupial (épipubic) bones, form the cartilaginous epiphysis of the pubic crest, and correspond to the supra-sternal ossifications ; the middle parts become the cartilaginous surfaces of the symphysis ; the posterior parts (the hypischium of reptiles) form the epiphyses on the pubic arch and ischial tuberosity (Parsons). On the other hand, Prof. Wingate Todd [8], who made a minute study of the symphysis pubis, particularly of the remarkable sequence of changes which occur in the human symphysis between the 20th and 40th years, is of the opinion that the epiphysis usually present on the cartilaginous surface of each side of the symphysis represents the whole length of the pelvic bar—anterior, middle and hinder parts. In most mammals the union at the symphysis ends in

Man's upright posture has thrown the duty of constantly supporting the shoulder on the trapezius. Under certain circumstances it gives way, the shoulders thus drooping. Symptoms may then arise from pressure of the nerves against the 1st rib, or a cervical rib [2].

Pelvic and Shoulder Girdles.—In the basal part of each limb bud a

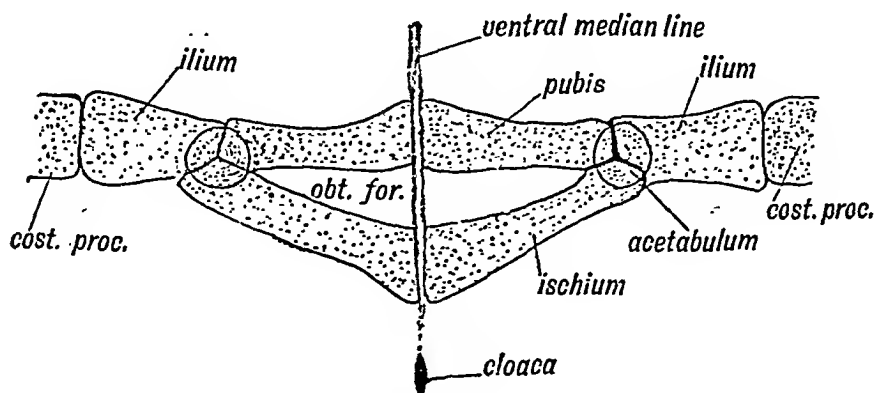


FIG. 539. Diagram of the Pelvic Girdle of a Lizard.

cartilaginous arch is developed. It consists of a *dorsal* and *ventral* part, the joint cavity for the articulation of the limb being situated at the junction of the two parts. Fishes retain this simple primitive form of girdle.

The *pelvic girdle* of man has undergone less modification from the

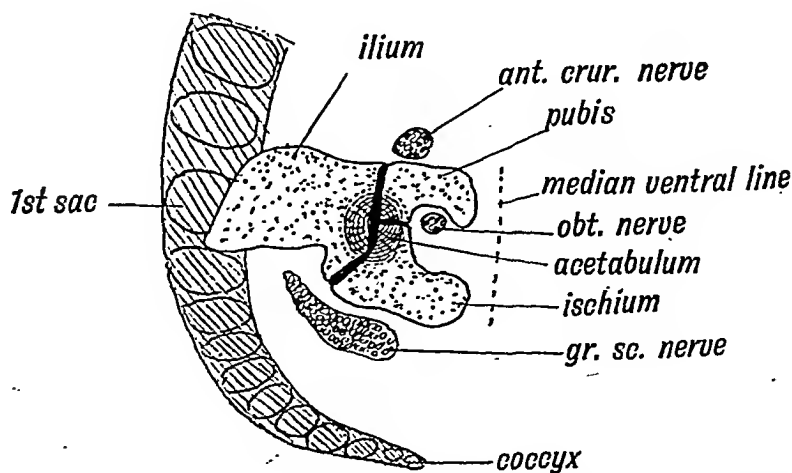


FIG. 540. The Pelvic Girdle of a Human Foetus at the 7th week. (After Kollmann.)

primitive type than his shoulder girdle. The primitive type of pelvic girdle, such as is seen in the crocodile or lizard, and of which the mammalian type is a derivative, is shown diagrammatically in Fig. 539. For comparison the human girdle in the 7th-week foetus is shown in Fig. 540.

The dorsal element consists of the *ilium*; it is attached by ligaments to the costal process of one or more sacral verteb

portion of the mesenchymal arch are developed two cartilaginous elements, the *pubis* and *ischium*, both of which take part in the formation of the acetabulum (Fig. 539). Both reach the ventral median line in which a median bar of cartilage is developed (see Fig. 516, B).

In man the following changes may be noted : (i) The costal processes of the sacral vertebrae ($2\frac{1}{2}$ usually) have fused together to form the lateral sacral mass ; with these the ilium articulates (Fig. 526) ; (ii) the vertebral border (crest) has become enormously elongated and gives attachment to abdominal muscles, cutting off the fibres of insertion of the external oblique which form the chief part of Poupart's ligament ; (iii) the ischium does not reach the ventral line. Up to the 4th month of development the bond between the ilium and sacrum is fibrocartilaginous in nature. In this bond there then are formed several synovial spaces, which subsequently fuse to form the synovial lining of the sacro-iliac joint [3]. The ligaments of the sacro-iliac joints, and particularly those of the symphysis, are sensitive to the action of oestrogens and undergo relaxation in the terminal months of pregnancy. This is especially true of animals which bear large-sized young, such as guinea-pigs [4]. The human ilium may effect contact not only with the costal elements of the sacrum but also with those which represent transverse processes [5].

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anchylosis; the human symphysis represents the persistence of an infantile stage. An intermediate stage of union is to be seen in the anthropoid pelvis (Todd).

Growth of the Pelvis.—As Dr. C. G. Payton has demonstrated [9], the pelvis undergoes extensive remodelling as it grows. Consider, for instance, the case of the obturator foramen. Were new bone to be laid down along its margin, the foramen would become progressively smaller, whereas it constantly increases in size during the years of growth, because as bone is deposited along one side of the foramen it is being absorbed with greater rapidity along the opposite border. The ilium grows in length at both its sacro-iliac and acetabular margins. Both acetabular and sacro-iliac joints are being constantly remodelled during the years of growth, especially at puberty. The sacro-iliac notch is fashioned by an absorption along the posterior (dorsal) border of the ilium. Growth of the true pelvis is effected at its three joints, namely, the right and left sacro-iliac and symphysis pubis. Growth at these joints is influenced by pituitary as well as by sex hormones. Amongst European women the antero-posterior diameter of the pelvic brim is greater than the transverse in 15% of cases [10].

Congenital Dislocation of the Hip Joint.—Under this title two quite different groups of cases are included: (i) cases in which there has been an arrest of development of the parts entering into the formation of the hip joint; (ii) cases which are produced during the act of delivery. It is only the first group which is referred to here. In the 8th week, when the foetus is about 20 mm. in length, the three cartilaginous elements—ilium, ischium and pubis—meet in a Y-shaped acetabular suture, the pubic element being later in chondrifying than the other two. In the 9th week the hip joint is formed by (i) the appearance of a synovial cavity; (ii) cartilaginous outgrowths from all three elements, but especially from the iliac, to form the acetabular cup; (iii) the separation of the head from the shaft of the femur by the formation of the neck (see p. 596). The joint is completely formed early in the 3rd month. The synovial lining of the joint arises from an ingrowth of peripheral cells into the blastemal tissue between the acetabulum and head of the femur [11]. The outgrowth of the acetabular brim may be arrested at the reptilian stage reached in the 2nd month; congenital dislocation of the femoral head, which as a rule is well formed, results. In the case of cleft palate and of imperforate anus (and this is a similar case) human development is arrested at a reptilian stage. The condition has a relation to the development of female sexual characters; 90% of cases occur in female infants. It is a sex-linked malformation, the defect being carried by one of the X chromosomes.

Shoulder Girdle.—The duckbill (ornithorhynchus) possesses the most generalized type of mammalian shoulder girdle; its girdle resembles closely that of primitive reptiles; from such a form the various types of mammalian shoulder girdle were probably evolved [12].

The main body of the bone about the 23rd year. The supra-spinous part of the scapula appears first in higher mammals; it is produced late in the development of the scapula (in the 3rd month of foetal life) by the upgrowth of the supra-spinous blade of the scapula; it is not represented in the pelvic girdle. The dorsal segment of the pelvic girdle

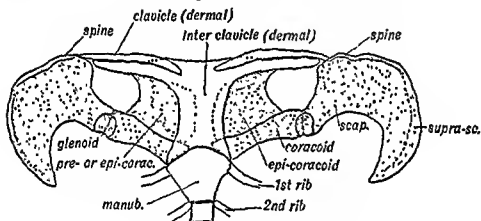


FIG. 541. The Shoulder Girdle of Ornithorhynchus.

becomes fixed to the costal processes; the corresponding part of the scapula remains free. The dorsal border of the scapula becomes more convex as age advances; in 35% of people it remains concave—giving the scaphoid type of scapula [13].

In the typical reptilian shoulder girdle, as in the pelvic (Fig. 539), two elements are formed in the ventral part of the arch—a posterior part, the coracoid, corresponding to the ischium, and an anterior, the precoracoid, corresponding to the pubis [14]. Both elements reach the ventral median line in which the sternum is developed (p. 582). In ornithorhynchus the coracoid element is represented by two bones—the coracoid and epicoracoid—the second of which is separated from the anterior end of the sternal bar during development and therefore corresponds to the suprasternal ossification of man. The dorsal extremity of the coracoid helps to form the glenoid cavity; its ventral articulates with the presternum. In man and all higher mammals, in which mobility

anchylosis; the human symphysis represents the persistence of an infantile stage. An intermediate stage of union is to be seen in the anthropoid pelvis (Todd).

Growth of the Pelvis.—As Dr. C. G. Payton has demonstrated [9], the pelvis undergoes extensive remodelling as it grows. Consider, for instance, the case of the obturator foramen. Were new bone to be laid down along its margin, the foramen would become progressively smaller, whereas it constantly increases in size during the years of growth, because as bone is deposited along one side of the foramen it is being absorbed with greater rapidity along the opposite border. The ilium grows in length at both its sacro-iliac and acetabular margins. Both acetabular and sacro-iliac joints are being constantly remodelled during the years of growth, especially at puberty. The sacro-iliac notch is fashioned by an absorption along the posterior (dorsal) border of the ilium. Growth of the true pelvis is effected at its three joints, namely, the right and left sacro-iliac and symphysis pubis. Growth at these joints is influenced by pituitary as well as by sex hormones. Amongst European women the antero-posterior diameter of the pelvic brim is greater than the transverse in 15% of cases [10].

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acromial process of the scapula to end ventrally in the anterior end of the sternal blastema. Prof. Fawcett found that during the 7th week, when the embryo is 15 mm. long, two centres of chondrification appear in the clavicular blastema, quite close to each other, one corresponding to the termination of fibres of the sternomastoid, the other to the ending of fibres of the trapezius. Before proper cartilage has had time to form, centres of ossification appear in the adjacent margins of the two pre-cartilaginous masses, the two ossific centres uniting in a few days. From this double centre ossification spreads during the 8th week towards the sternum and towards the acromion, ossification being preceded by a formation of true cartilage [16].

There is a malformation of the clavicle which throws light on its double nature. In the remarkable disorder of growth known by the cumbersome name of *cleido-cranial dysostosis* [17] the clavicle is made up of two parts, an outer and inner united by a fibrous band, which may form only a short ligament, or may be so extensive as to represent the middle two-thirds of the bone. In such cases all the bones of the skeleton which are formed in membrane—especially those of the cranial vault—are imperfectly ossified. The condition in this disease suggests that the clavicle is a compound bone made up of outer and inner elements, and that arrest has occurred before the two elements have become joined. In cleido-cranial dysostosis a disturbance occurs which prevents the union of the two ossific centres of the clavicle; as ossification in cartilage proceeds normally in other parts of the skeleton we may presume that in spite of the appearance of cartilage in the clavicle, it was originally a membranous bone.

The acromion process is ossified from several centres which appear in the years of adolescence; the epiphysis so formed may be united to the spine by fibrous tissue only. This occurs in over 8% of subjects (Symington), and may be mistaken for a fracture of the process. The coracoclavicular ligaments may be derived from the precoracoid element.

Hand and Foot.—The hand and foot of man, as is the case in all primates, retain the primitive arrangement of elements much more closely than do most other mammalian orders. The primitive type of hand or foot, out of which the various forms found in mammals have been modified, is seen in such reptiles as the lizard or tortoise (Fig. 543). In the hand of man the same bones are to be seen as in the tortoise, and in the same order of arrangement, with some exceptions. The elements in the foot of a typical lizard resemble closely the arrangement seen in its hand; the same elements are present even in the highly modified human foot (Fig. 544). The hand and foot bones have undergone great specialization in most mammals. In the evolution of the horse, for

of the fore limb is of advantage for speed and free movement, the coracoid element is much reduced. It forms merely a process on the scapula, which it joins in man about the 15th year. It still enters into the formation of the glenoid cavity, the articular part (supra-glenoid) having a separate centre of ossification which appears in the 12th year. It is possible that the costo-coracoid ligament may be derived from the ventral part of the coracoid element—the part which articulates with the sternum in the duckbill. The precoracoid in the shoulder girdle of a lizard corresponds to the pubic element in the pelvis. The precoracoid, which, like all the primitive elements of the pelvic and shoulder girdle, is formed in cartilage, has been partly or entirely replaced in all mammals by the development over it of the clavicle, a dermal or membrane-

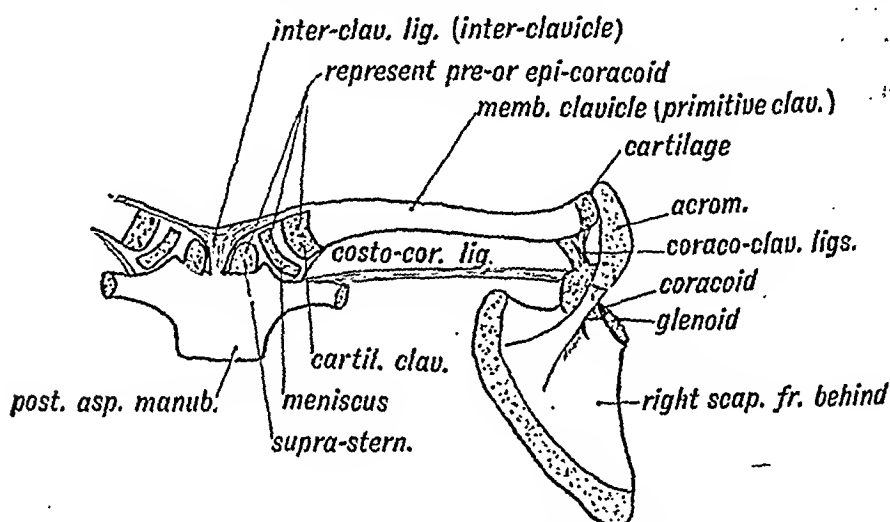


FIG. 542. The Parts in the Shoulder Girdle of a Human Foetus which correspond with those of Ornithorhynchus.

formed bone, the first of all the bones to ossify. In certain fishes the cartilaginous shoulder girdle has a covering of membranous (dermal) bone; from this dermal covering the clavicle and interclavicle have been evolved [15]. There is thus no true representative of the clavicle in the pelvis. The interclavicle so strongly developed in ornithorhynchus and in the "merry-thought" of the fowl is also a dermal bone. It is represented in man by the interclavicular ligament.

In order to give greater mobility and speed to some four-footed mammals, the clavicle has been reduced to a ligamentous band, except at its extremities (rabbit, dog, etc.). In climbing animals and those in which the power of grasping or embracing is highly developed the clavicles are fully developed.

Clavicle.—At the beginning of the 7th week the clavicle is represented by a cellular or blastemal bar passing from the neighbourhood of the

sponding hands form the middle and posterior fasciculi of the external lateral ligament.

4. *Carpale or Tarsale I* becomes the trapezium in the hand, the internal cuneiform in the foot. In the prehensile foot of apes, the hallucial articular surface is widely separated and directed inwards. This is also the case during the foetal development of the human foot, but at no period of development is the hallux of man directed inwards and separated from the other toes. In man the great toe resumes a primitive position, its metatarsal coming into line with other members of the metatarsal series.

5. *Carpale or Tarsale II* forms the trapezoid in the hand, the middle cuneiform in the foot.

6. *Carpale or Tarsale III* forms the os magnum (os capitatum) in the hand, the external cuneiform in the foot.

7. *Carpale or Tarsale IV and V* have united in hand and foot to form

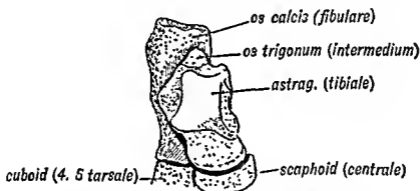


FIG. 545 The Os Trigonum and other Bones of the Tarsus

the unciform and cuboid. This occurs in all mammals. The unciform process has a separate centre of chondrification (Lewis). In the cat and other carnivores the scaphoid and semilunar unite together, a union which may occur in man. Union of trapezoid to the os magnum has also been reported [19]. In the foot an intimate union persists at the junction of the os calcis, cuboid and scaphoid until late in the 3rd month; in the cartilage of union a separate tarsal element (secondary os calcis or secondary cuboid) may develop [20].

The *Os Centrale* [21] is situated between the first and second rows of the carpal or tarsal bones (Fig. 543). In the primitive carpus the centralia were four in number (Fig. 546, A). In the foot an os centrale forms the scaphoid—a bone which plays an important part in the formation of the plantar arch—but is yet remarkably late in beginning to ossify, viz. about the 3rd year. It appears at the end of the 6th week as a separate cartilage element of the human carpus, but at the end of the

instance, one lateral digit after another has become vestigial, leaving the central digit enormously enlarged and specialized to form the lower part of the extremities. In ruminants the 3rd and 4th digits have become dominant; the rest of the digits have become reduced until only traces of them are left [18]; in rodents the hallux is vestigial. The hallux and pollex are the mammalian digits most liable to undergo retrogression. In man, on the other hand, the hallux and pollex find their greatest development.

Comparison of the Tarsus and Carpus.—Both are the derivatives of such a typical form as is shown in Fig. 543. In the typical tarsus or carpus there occur the following bones:

1. *Radiale or Tibiale* forms the scaphoid (naviculare) in the hand and

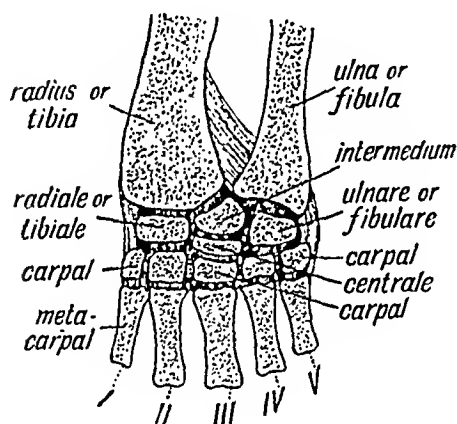


FIG. 543.

FIG. 543. The Carpal Bones of a Tortoise.

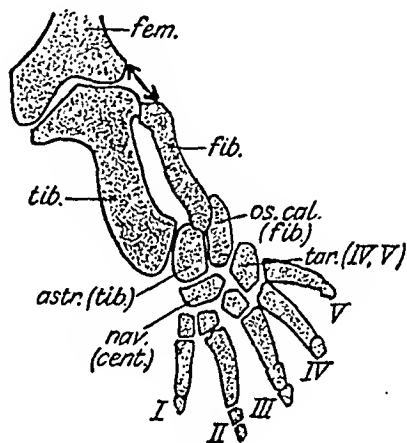


FIG. 544.

FIG. 544. The Skeletal Elements of the Leg and Foot of a Human Foetus in the 9th week. The double arrow indicates the earlier relationship of fibula to femur. (Bardeen.)

astragalus in the foot. In the human hand this bone is occasionally double, being formed from two centres. The astragalus in the early human foetus (Fig. 544) occupies the position of the intermedium.

2. *Intermedium* forms the semilunar (os lunatum) in the hand; in the foot it is much reduced and usually unites with the astragalus to form the external tubercle of that bone. It may remain separate and form the *os trigonum* (Fig. 545).

3. *Ulnare or Fibulare* becomes the cuneiform (triquetrum) in the hand, the os calcis in the foot. During the mesenchymatous and early cartilaginous stages in the development of the human tarsus, the os calcis is in contact with the fibula (Fig. 544). In the hand the ulnare and intermedium are bound by fibrous bands to the ulna (Fig. 543); these bands assist to form the triangular fibro-cartilage; in the ankle the corre-

the pisiform of the human hand being a displaced centrale (Fig. 546, A, B). The gastrocnemius, which represents the flexor carpi ulnaris in the leg, is also primitively a flexor of the metatarsus; the long plantar ligament, from which it is separated by the growth of the heel, represents the continuation of its tendon.

Anomalous Ossification of the Foot [23].—In Fig. 547, A, a diagram is given of the bones of the foot to show the more common sites of anomalous ossifications. Of these the os trigonum and the secondary calcaneum and secondary cuboid have already been mentioned. On the outer or fibular

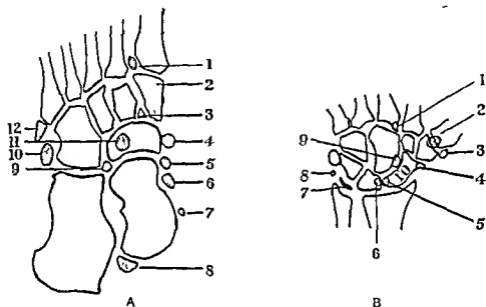


FIG. 547.

border of the foot three ossifications may be met with: (i) the bone of Vesalius, situated at the base of the 5th metatarsal. The styloid process of this bone has occasionally a centre of ossification (Flecker); the bone of Vesalius may be a separate formation of this epiphysis; (ii) on the outer border of the cuboid—an ossification, os peroneale, of uncertain nature; (iii) ossification of the sesamoid within the tendon of the peroneus longus. On the inner or medial border of the foot the most common site is below the tuberosity of the navicular bone (os tibiale). The navicular may be ossified from two centres [24]. The internal cuneiform may be double; its distal articular surface, like the corre-

2nd month it has joined the dorsal and distal aspect of the scaphoid of the hand. It may be occasionally detected as a tubercle on the dorsal aspect of the scaphoid, or even as a separate bone. It is a separate bone in the carpus of all primates except the gorilla, chimpanzee and man. There are two or more centralia in lower vertebrate forms (Fig. 546). The styloid process at the base of the 3rd metacarpal bone may occur as a separate ossification (*os styloideum*, Fig. 547, B).

The *Pisiform* is of doubtful nature. It is possible that in a very early stage of the evolution of mammals there were more than five digits: one behind the little finger—post minimal digit; and another on the radial side of the hand—a prehallux [21]. Supernumerary digits, when they appear, are commonly situated on the radial side of the thumb or

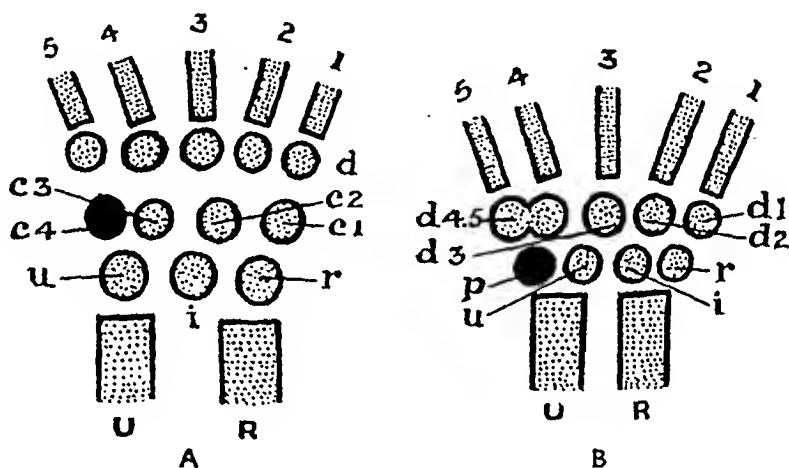


FIG. 546.

- A. Showing the four Centralia of the Primitive Vertebrate Hand. (C. D. Gillies.)
 B. Showing the possible Origin of the Pisiform from a displaced Centralia. (C. D. Gillies.)

U, ulna; R, radius; d, distalia (1, 2, 3, 4, 5); u, ulnare; r, radiale; i, intermedium centralia, 1, 2, 3, 4—the 4th being represented in black; p, pisiform.

ulnar side of the little finger, but they usually represent merely a fission of the normal pollex or little finger. The pisiform has been regarded as the vestige of a post minimal digit; the sesamoid on the trapezium, in which a slip of the extensor ossis metacarpi pollicis ends, as a remnant of a prehallux. It is possible also to regard the pisiform as a sesamoid developed in the tendon of the flexor carpi ulnaris—for that muscle is originally a flexor of the metacarpus and ends on the 5th metacarpal—the piso-metacarpal ligament representing the terminal part of the tendon. The pisiform, however, is developed with the rest of the carpal bones and before the tendon of the flexor carpi ulnaris. In mammals generally, but not in man, the pisiform articulates with the ulna as well as the cuneiform, and its synovial facet opens into the wrist joint. Dr. C. D. Gillies [22] has brought forward evidence in favour of regarding

and well developed in man only. It is developed from the outer and lower fibular fibres of the extensor longus digitorum and represents part of the tendon of that muscle to the 5th toe. The peroneus hrevis and longus may also assist, especially the latter, which in apes is a grasping muscle, acting as a flexor of the metatarsal bone of the hallux.

(ii) The tarsal bones of the human foot—especially the astragalus and os calcis—are of great size when compared with the tarsal bones of other primates; while the digital or phalangeal elements, except in the case

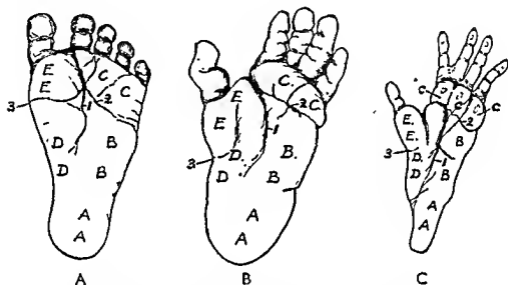


FIG. 549.

A The Plantar Aspect of the Foot of a Child at birth, showing the flexure lines.

B Plantar Aspect of the Foot of a Gorilla

C Plantar Aspect of the Foot of an Old-world Monkey.

1 Oblique flexure line; 2, transverse flexure line, 3, thenar flexure line. A, B, C, D, E, these letters indicate corresponding plantar areas

of the great toe, which is relatively of great size, have undergone retrogression. This is especially the case in the human little toe; some of its muscles are not infrequently fibrous, and the terminal phalanx may not be separated from the middle phalanx. The middle (2nd) phalanx is the last to be differentiated in development of the fingers and toes (in 3rd month).

(iii) The plantar arches [28], both longitudinal and transverse, come into existence in early foetal life. The arch of the foot is a human character. At birth a child is flat-footed *when the weight of the body rests on its feet*; the head of the astragalus is then on a level with the entocuneiform. When the muscles are removed by dissection the foot of the newly born child shows a well-developed arch (Russell Howard).

sponding articulation on the first metatarsal, may be divided, partially or completely, into a dorsal and a plantar area [25].

Eversion of the Foot and Development of the Arch.—The human foot has been highly modified for upright progression [26]. The chief modifications are :

(i) Gradual *eversion* of the foot, so that the sole can be applied to the ground. Even at birth—and for some time after—and always up to and before the 7th month of foetal life, the soles of the feet are inverted, so that when the foetal limbs are in their natural position they are directed towards the belly of the child. In *club foot* the normal process of eversion does not take place; *club foot*, like cleft palate, represents an arrested development [27]. The ape's foot retains the inverted position, an

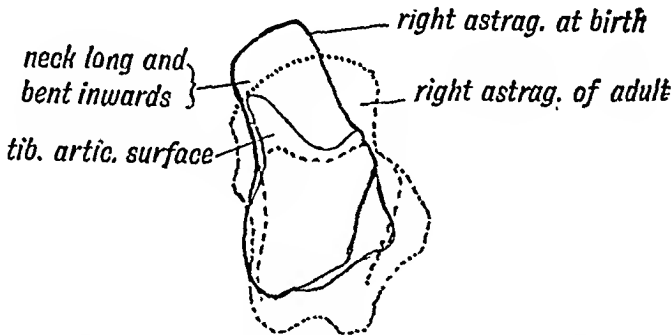


FIG. 548. The Foetal and Adult (in dotted outline) Forms of the Astragalus contrasted.

adaptation for prehension. The following factors assist in producing eversion :

- (a) The neck of the astragalus (Fig. 548), which in the foetal foot is long and directed downwards and inwards at an angle to the axis of its body, becomes relatively shorter and directed more in line with the axis of the articular surface of its body. Further, the lateral border of the tibial articular surface of the astragalus is prominent in the foetus; the medial border is much the lower; a growth upwards of the medial border causes the astragalus and foot to rotate outwards (Lazarus). A special process is produced at the dorso-lateral angle of that surface of the os calcis which articulates with the cuboid. This process limits the extent of eversion [28].
- (b) The bones on the inner side of the foot, particularly the scaphoid and internal cuneiform, grow more rapidly than those on the outer side of the foot—especially after birth. This tends to evert the foot and also to produce the longitudinal arch.
- (c) A special evertor of the foot is produced—the peroneus tertius—a muscle which occurs in the gorilla as a variation, but is constant

brevis or *primi internodii pollicis* is constant in man only [30]; it is a segment of the *extensor ossis metacarpi pollicis*. The *extensor brevis hallucis*, which is a medial slip from the *extensor digitorum brevis*, is not represented in the hand.

Muscles of the Second Digit.—In the lower primates each finger has two extensors—a deep and superficial. The deep in the second digit becomes the *extensor indicis*; in the little finger it forms the *extensor minimi digiti*. The deep extensor muscles have disappeared in man from the 3rd and 4th digits, but occasionally reappear. In the leg the deep extensors have migrated to the foot, and form the *extensor brevis digitorum*. That for the little toe, however, has not descended; it is always vestigial, if present. It runs beneath or with the *peroneus brevis*, and is known as the *peroneus quartus* or *peroneus quinti digiti*. If the mirror-image theory is true it represents the *extensor brevis pollicis* [31].

Flexors and Extensors of the Metacarpus.—These have retained their primitive insertions in the hand; their modifications in the foot have been already mentioned [32]. Both at the knee and elbow joint the origins of these muscles have undergone much shifting and migration.

Migration of Muscular Attachments.—Many human muscles during development acquire attachments to segments at a distance from those in which they are developed. The *serratus magnus* is developed from 5th, 6th, 7th cervical segments: its attachment has extended backwards until, in man, it reaches the 8th rib; the *trapezius*, originally situated in the neck, migrates backwards, and in the 7th week obtains an insertion to the shoulder girdle, and before the end of the 3rd month its origin has reached as far backwards as the 12th dorsal spine along the median dorsal line. The *latissimus dorsi* migrates to the median dorsal line over the spinal musculature and reaches the spine and crest of the ilium. The *diaphragm*, which arises in the neck (4th and 5th segments), descends until it is attached in the floor of the thorax. The facial musculature takes its origin in the hyoid arch. The subvertebral (hypaxial) musculature is a migrant part of the transversalis sheet. The *omo-hyoid* is attached at first to the sternum; it migrates along the clavicle and reaches (often it fails to reach) the upper border of the scapula. The *migration of the subclavius* has been in an opposite direction; originally it reached to the humerus. The case of the *extensor brevis digitorum* of the foot has just been mentioned. The *flexor accessorius* is a part of the *flexor longus hallucis* which has migrated to the sole of the foot. The *opponens* of the thumb and of the little finger are separated parts of the short flexor muscles of these digits. These are only a few of the more striking examples of the migration in the attachment of muscles

The arch becomes stable as the child learns to walk. The chief factors in its production are the growth of the tarsal bones—especially of the scaphoid and internal cuneiform—and 1st metatarsal and the co-ordinated (postural) action of the muscles of the leg and foot. Hence in rickets, where the normal tarsal growth is disturbed, flat foot is apt to occur. Amongst the structural changes which help to maintain the arch are :

- (a) The growth of the os calcis backward to form the heel separates the tendon of the plantaris from its prolongation in the sole—the middle part of the plantar fascia, which assists in maintaining the arch. In lower primates the two parts are continuous, the tendon of the plantaris plying across the os calcis in a cartilage-lined groove.
- (b) The internal lateral ligament of the ankle (anterior part) and the inferior calcaneo-scaphoid ligaments undergo a great development in man [29].
- (c) The flexor brevis digitorum, which in lower primates arises principally from the long flexor tendons in the sole, has its origin completely transferred to the os calcis in man. It can thus act more powerfully in maintaining the arch. The flexor accessorius, a detached part of the flexor longus hallucis, is specially well developed and helps to maintain the arch of the foot.
- (d) The tibialis posticus, originally a flexor of the metatarsus, corresponding to the flexor carpi radialis in the hand, obtains a secondary attachment to the scaphoid. The tibialis anticus, which answers to the extensor ossis metacarpi pollicis, becomes permanently inserted into the internal cuneiform and metatarsal. Both of these muscles, thus modified, help to maintain the arch of the foot. So does the tarsal part of the tendon of the tibialis posticus.
- (e) The long plantar ligament—originally a part of the tendon of insertion of the gastrocnemius—also assists to maintain the arch.
- (iv) The development of the great toe and the peculiar arrangement of its muscles must also be regarded as adaptations in the foot to upright posture and progression.

CERTAIN FEATURES OF THE MUSCULATURE OF HUMAN LIMBS

Muscles of the Pollex and Hallux.—The extensor ossis metacarpi pollicis corresponds to the tibialis anticus. The thumb muscle has commonly a carpal insertion as well as a metacarpal. The extensor

borders of the pectoralis major and latissimus dorsi, are parts of the muscular sheet out of which these two muscles are developed.

(iv) The *pectoralis externus* arises from the 4-5-6 ribs and costal cartilages, beneath the axillary border of the pectoralis major. This is its normal condition in most mammals, but in man it is commonly fused with, and forms part of the pectoralis major.

(v) The *sternalis* is a remnant of the primitive rectus sheet (p. 495). The pectoralis major is formed from the same ventral longitudinal sheet as the rectus abdominis and sterno-mastoid. The fibres of the sternalis, which lie along the sides of the sternum, superficial to the origin of the pectoralis major, represent a persistent part of the primitive longitudinal sheet.

(vi) In the *sterno-mastoid* four elements are recognized: sterno-mastoid, sterno-occipital, cleido-mastoid, cleido-occipital. The cleido-occipital fibres, which form part of the same sheet as the trapezius, are often absent. On the other hand, the cleido-occipital fibres may be continuous with the trapezius. The *sterno-mastoid* and *trapezius* muscles are developed from the ventral element of occipital segments } and are originally connected with gill arches.

(vii) The *pectoralis minor* is sometimes inserted in the capsule of the shoulder and great tuberosity of the humerus, as is the case in primates generally. The coracoid insertion, which is the normal one in man and also in the gorilla, is usually regarded as a secondary attachment, but Dr. K. Lander [34] has shown that it is also found in primitive types of mammals. When the pectoralis minor is inserted to the coracoid, the former fibres of insertion become fused with and form part of the coraco-humeral ligament, which, however, is a distinct structure, and represents a specialized part of the capsule of the shoulder joint.

(viii) In some apes (such as the Gibbons) the *biceps* has four heads—the two usual, the long and short, and two others, one from the inner border of the humerus and one from the bicipital groove. These two extra heads appear frequently in man. The tendon of the long head is developed within the cavity of the shoulder joint (Neale).

(ix) The *epitrochleo-anconeus* is often present. It crosses the ulnar nerve from the internal condyle to the olecranon [35].

(x) The *palmaris longus* and its homologue in the leg, the *plantaris*, are vestigial, aberrant in form and often absent. The plantar and palmar fasciae represent their divorced tendons. The plantaris and palmaris undergo retrograde changes in the primates with the transformation of claws to nails [36].

(xi) Each digit (fingers and toes) in lower primates, such as monkeys, is provided with three short muscles which arise from the carpus or tarsus.

but the mechanism which brings about migration and the biotactic influence which is at work are unknown.

Vestigial and Abnormal Muscles of the Limbs and Trunk.—(i) The muscles of the human *ear and scalp* may be described as vestigial when compared with their development in other mammals. Although their action on the ear and scalp is feeble, yet they serve as an important basis into which certain psychological states are reflected.

(ii) The *levator claviculae* (omo-trachelian) is a muscle which passes from the upper transverse cervical processes to the outer end of the clavicle or acromion process. It is well developed in climbing primates.

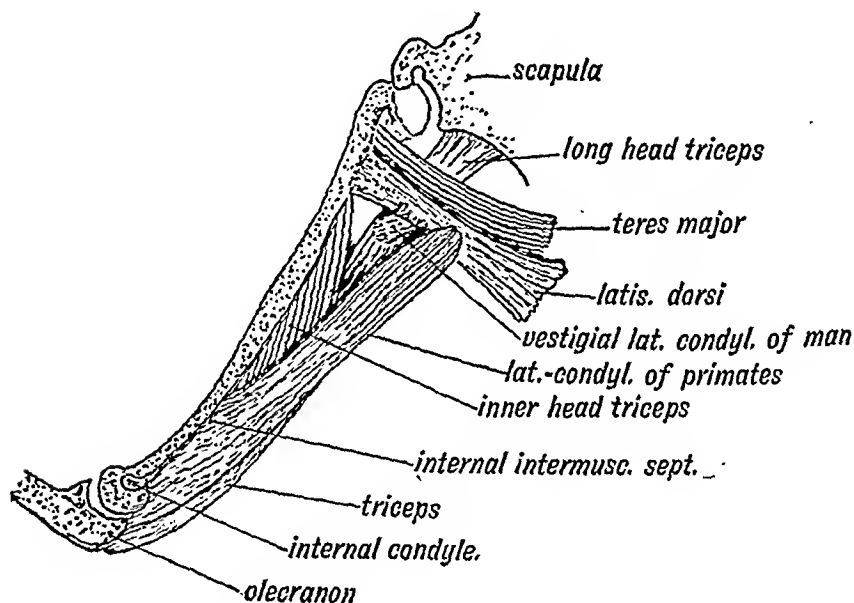


FIG. 550. Latissimo-condyloideus Muscle.

It is not a common muscle in man. It can be recognized during life in the posterior triangle of the neck.

(iii) The *latissimo-condyloideus* (dorso-epitrochlearis) [33], a climbing muscle, is always represented in man, commonly by a fibrous bundle between the tendon of the latissimus dorsi and the long head of the triceps (Fig. 550). This fibrous strand may be occasionally muscular. In apes it passes from the latissimus dorsi at the axilla to the inner aspect of the elbow and arm, which it retracts in climbing. It belongs to the same sheet as the coraco-brachialis. The *ligament of Struthers*—a strip of fibrous tissue over the internal intermuscular septum, above the internal condyle—represents part of the tendon of this muscle. The muscular slips occasionally found crossing the brachial or axillary artery from the latissimus dorsi to the coraco-brachialis or biceps are derivatives. Other slips found crossing the floor of the axilla, between the adjacent

muscular sheet which forms the peroneal muscles. Amongst primates, the short head is found only in man, the anthropoids and some South American apes. It corresponds to the brachialis anticus in the arm, and is supplied by the external popliteal nerve.

(xvi) The *psoas parvus* is also vestigial. It acts primarily as a flexor of the pelvis on the spine. It begins to disappear in those primates which assume the erect posture [38].

(xvii) The *scansorius* is a separated segment of the gluteus medius and minimus. It rises from the anterior border of the ilium and passes to the great trochanter. It corresponds to the teres minor. It is not constant in any animal.

(xviii) The *flexor brevis digitorum* to the little toe and the adductor transversus of the great toe are often fibrous.

Sesamoids [39]—The digital sesamoids of the human hand and foot

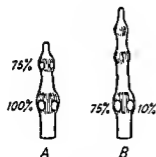


FIG 552.

FIG 552 A. Frequency of Sesamoids in Thumb and Great Toe.

B Frequency of Sesamoids in 2nd Digit of Hand and Foot

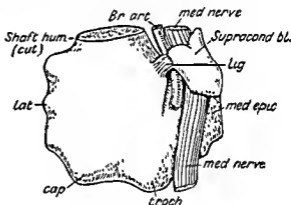


FIG. 553.

FIG 553 Distal end of Right Humerus (flexor aspect) of a Human Foetus in the 7th week of development. (Kozlik.)

Supracond. bl., blastema of supracondylar process; *lig*, ligament uniting it to humerus, *med. ner*, median nerve; *Br. art.*, brachial artery; *med. epic*, median epicondyle.

are subject to varying degrees of constancy. They are constantly present in only two joints, the metacarpo-phalangeal joint of the pollex and that of the hallux. They are developed in the volar and plantar ligaments of these two joints, their deep surface plying on the articular head of the metacarpal or metatarsal bone. They are more frequently present than absent in the interphalangeal joint of the hallux and pollex (Fig. 552, A). Sesamoids also occur in the metacarpo-phalangeal joints of other digits, that on the radial or tibial side of the 2nd digit being the most frequently present (Fig. 552, B). They are usually absent on the ulnar or fibular side of the other digits.

The three muscles are (Fig. 551): (i) a short flexor on the radial side of the digit; (ii) a short flexor on the ulnar side; (iii) a *contrahens* or adductor muscle (always absent in the middle digit). The ten short flexor muscles form a deeper sheet than the four *contrahentes*. Of this form the arrangement of the short muscles in the human hand is a derivative. The remnants in the human hand and foot of the *contrahentes* are: (i) the adductors of the 1st digit (pollex or hallux); (ii) fibrous remnants of the others occur over the deep plantar or carpal arch (Fig. 551). The short flexors in man have become (i) the seven interossei; (ii) the flexores breves (ulnar and radial) and opponens of the 1st digit; the flexor brevis and opponens of the 5th digit (see Fig.

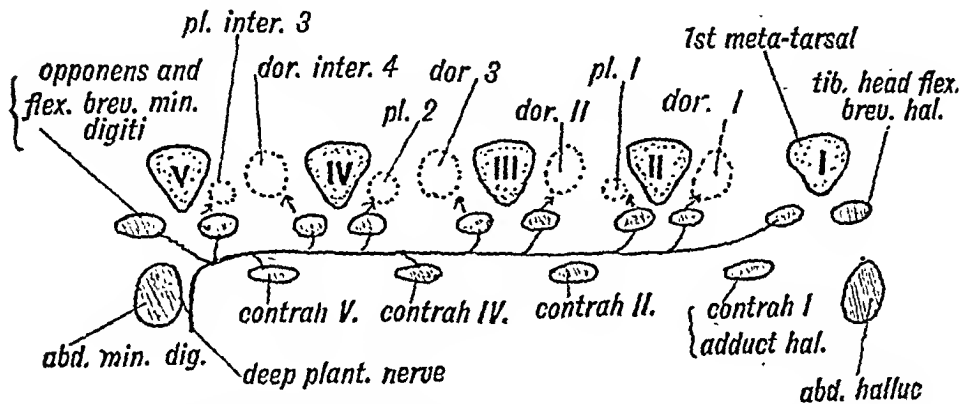


FIG. 551. The Morphology of the Short Muscles of the Digits. The muscles shaded are those of the ape's hand or foot; the positions of the corresponding muscles in the human hand or foot are indicated by dotted outlines.

551). The ulnar flexors of the thumb and great toe are absent or fibrous.

(xii) The *pyramidalis* is often absent in man or vestigial. It is the tensor of the linea alba.

(xiii) Remnants of the *extensors* and *flexors* of the tail may occur between the sacrum and the coccyx (p. 570).

(xiv) The *coccygeus* is vestigial; its superficial part forms the small sacro-sciatic ligament.

(xv) Fibres of the biceps of the thigh may be followed into the *great sacro-sciatic ligament*. This ligament, which is almost peculiar to man—in other primates it is quite thin and slender—may contain fibres derived from the caudō-femoral group of muscles, such as the *tenuissimus*, a long strap-like muscle which passes from the coccyx to the femur and leg in lower mammals. The sacro-sciatic ligament is mainly derived from the great median sheet, out of which the middle layer of the lumbar fascia is also formed. Parsons regards the *short head* of the *biceps* as a derivative of the *tenuissimus*, while others regard it as part of the

[16] For development of clavicle, see Fawcett, E., *Jour. Anat.*, 1913, 47, 225; Rutherford, N. C., *ibid.*, 1914, 48, 355; Hanson, F. B., *Anat. Rec.*, 1930, 19, 309; Brandt, W., *Zeitsch. Anat. Entwickl.*, 1935, 104, 653 (remodelling of acromial end); Parsons, F. G., *Jour. Anat.*, 1917, 51, 71 (sex and other markings of clavicle).

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[18] Harris, H. A., *Nature*, 1936, 133, 928.

[19] Cave, A. J. E., *Jour. Anat.*, 1926, 60, 461.

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[21] For plans of hand and foot of primitive vertebrates, see Gregory, W. K., *Bull. Amer. Mus. Nat. Hist.*, 1923, 48, 279; Howell, A. B., *Jour. Morph.*, 1935, 57, 105 (elements of carpus and tarsus); Schultz, A. H., *Quart. Rev. Biol.*, 1936, 40, 259, 425 (carpus and tarsus of apes). For extra or abnormal elements, see Forster, A., *Archiv. d'Anat.*, 1933, 17, 387 (epilunar and hypolunar elements); Nayak, U. V., *Jour. Anat.*, 1934, 68, 109; Bruno, G., *Anat. Anz.*, 1935, 79, 390 (os styloideum); Dupas and Badelon, *Ann. d'Anat. Path.*, 1932, 9, 335; Cordebar, J., *ibid.*, 1938, 15, 65 (os styloideum); Bayer, F., *Zeitsch. Anat. Entwickl.*, 1934, 103, 634 (bipartite scapoid); Partridge, E., *Jour. Anat.*, 1923, 57, 378 (divided trapezoid). For extra digits, see Cummins, H., *Amer. Jour. Anat.*, 1932, 51, 381; Nylander, E. S., *Upsala Laekar. Foerhandl.*, 1931, 36, 275 (inheritance).

[22] Gillies, C. D., *Jour. Anat.*, 1920, 63, 380.

[23] For abnormal ossification of foot, see Holland, C. T., *Jour. Anat.*, 1921, 55, 235; Bizarro, A. H., *ibid.*, 1921, 55, 256; Pfitzner, W., *Morph. Arbeiten*, 1896, 6, 245; Dwight, T., *Variations of the Bones of Hand and Foot*, 1907.

[24] Flecker, H., *Jour. Anat.*, 1933, 67, 118.

[25] Barclay, M., *Jour. Anat.*, 1933, 67, 175 (double entocuneiform); Boeker and Mueller, *Anat. Anz.*, 1936, 83, 193 (divided articular surface).

[26] For evolution of human foot, see Keith, Sir A., *Jour. Bone Joint Surg.*, 1929, 11, 1; Morton, Dudley J., *ibid.*, 1924, 6, 56; *The Human Foot*, 1935; Schultze, A. H., *Amer. Jour. Phys. Anthropol.*, 1930, 14, 85; *Quart. Jour. Biol.*, 1936, 11, 440; Strauss, W. L., *Contrib. Emb.*, 1927, 19, 93 (growth of foot before birth); Davenport, C. B., *Amer. Jour. Phys. Anthropol.*, 1933, 17, 167 (growth after birth).

[27] Man, C., *Archiv. Orthop. Unfall Chir.*, 1930, 29, 292 (club-foot as an arrest of development); Browne, Dennis, *Proc. Roy. Soc. Med.*, 1936, 29, 49 (sect. Dis. Children); Keith, Sir A., *Brit. Jour. Surg.*, 1940, 28, 173.

[28] Bruce, J., and Walmsley, R., *Lancet*, 1938, 2, 656 (development of arches of foot); Elftman and Manter, *Jour. Anat.*, 1936, 70, 56 (limitation of eversion by articulation of os calcis); Williams, G. A., *Amer. Jour. Phys. Anthropol.*, 1931, 16, 1 (development of powers of inversion and eversion).

[29] For description of ligaments in simian foot, see Keith, Sir A., *Jour. Anat.*, 1894, 28, 149; Stamm, T. T., *ibid.*, 1932, 66, 80 (ligamentum cruciatum).

[30] McGregor, A. L., *Jour. Anat.*, 1926, 60, 259.

[31] See under note [14].

[32] McMurrich, J. P., *Amer. Jour. Anat.*, 1906, 6, 407 (muscles of foot); *ibid.*, 1904, 4, 33 (muscles of thigh).

[33] Fitzgerald, R. R., *Jour. Anat.*, 1936, 70, 273 (dorso-epitrochlear muscle in living child).

[34] Lander, Kate, *Jour. Anat.*, 1918, 52, 292; Davies, F., *ibid.*, 1935, 69, 132; Seib, C. A., *Amer. Jour. Phys. Anthropol.*, 1933, 23, 389; Fang-D-chau, *Zeitsch. Morph. Anthropol.*, 1937, 37, 119.

The *Supra-condylar Process* [40] is well developed in lemurs, the lowest primates, and in mammals of many orders. Its function is unknown. It occasionally appears in man. Dr. N. C. Rutherford found it represented in a human foetus in the 9th week of development. It is developed from a separate blastema which appears above the medial epicondyle, on the superficial aspect of the brachial artery and median nerve (Fig. 553). The blastema is united to the epicondylar ridge by a ligamentous band. If the humeral end of this band ossifies a hook-like process is formed; if the band and blastema ossify, then a supra-condylar foramen is produced. Usually such processes are hook-shaped and lie in front of the internal intermuscular septum. If a process is strongly developed, the brachial artery and median nerve pass under it, as they do in such animals as the squirrel and cat.

NOTES AND REFERENCES

[1] Congenital elevation of the scapula is often spoken of as "Sprengel's shoulder"; see Fairbank, H. A. T., *Brit. Med. Jour.*, 1911, 2, 1533.

[2] Todd, T. Wingate, *Anat. Anz.*, 1912, 41, 385.

[3] Hakin, M., *Ann. d'Anat. Path.*, 1937, 14, 466.

[4] Ruth, E. B., *Anat. Rec.*, 1937, 67, 409; see also references given in note [8].

[5] Seligman, S. B., *Anat. Anz.*, 1935, 79, 225; Trotter, M., *Amer. Jour. Phys. Anthropol.*, 1937, 22, 247; Stewart, T. D., *ibid.*, 1938, 24, 43; Brooke, R., *Proc. Roy. Soc. Med.*, 1934, 27 (9), 1211 (mobility of sacro-iliac joint).

[6] Ruth, E. B., *Anat. Rec.*, 1932, 53, 207.

[7] Patje, A., *Zeitsch. Morph. Anthropol.*, 1934, 34, 321.

[8] Todd, T. W., *Amer. Jour. Phys. Anthropol.*, 1920, 3, 285; 1921, 4, 1 *et seq.*; *Jour. Anat.*, 1923, 57, 274; *Amer. Jour. Anat.*, 1923, 31, 355 (relaxation of symphysis pubis in pregnant guinea-pigs).

[9] Payton, C. G., *Jour. Anat.*, 1935, 79, 326.

[10] Greulich, W. W., *Anat. Rec.*, 1938, 70, 33 (suppl. 3); Nicholson, C., *Jour. Anat.*, 1945, 79, 131, 503 (diameters of female pelvis).

[11] Platt, H., *Lancet*, 1939, 1, 393 (280 cases reviewed, 85% being female); Pratje, A., *Anat. Anz.*, 1936, 81, 229 (suppl.).

[12] Broom, R., *The Mammal-like Reptiles of South Africa*, 1931.

[13] Graves, W. W., *Amer. Jour. Psychiat.*, 1937, 93, 1109.

[14] I have repeated the statement made in previous editions, but the reader will see that if the mirror-image theory (p. 598) is true, then the coracoid should be compared not with the ischium but with the pubis, and the epicoracoid element with the ischium. The coracoid of reptiles represents the epicoracoid of ornithorhynchus (Romer, A. S., *Anat. Rec.*, 1922, 24, 39). It is probable that the epicoracoid element is represented in man by the suprasternal ossification of the manubrium. Prof. D. M. S. Watson has observed that in the evolutionary history of the shoulder girdle the precoracoid is the first element to reach the mid-ventral or sternal line and that later it is supplanted by the coracoid element, see p. 615.

[15] Gregory, W. K., *Proc. Amer. Phil. Soc.*, 1936, 76, 429.

CHAPTER XXXI

DEVELOPMENT OF BONES AND JOINTS

In this chapter, which is the third devoted to a consideration of the development and morphology of the human limbs, the two chief subjects that are to engage our attention are: (1) the development and morphology of their joints; (2) the manner in which their bones are formed and the modes by which they grow and change. We shall also have to examine briefly the present state of our knowledge concerning the activities and life-histories of bone-forming cells.

Development of Joints [1].—Each limb bone is formed from a centre of chondrification which appears in the 2nd month within the unjointed skeletal blastema of the limb bud. At these centres the mesodermal cells gradually assume the characters of cartilage cells; growth proceeds most rapidly at the periphery of the cartilage centres; as the growing centres approach each other, part of the original blastema is left between them. This tissue, which may be named the *interchondral disc*, forms the first basis of a joint (Fig. 554). The cells in the peripheral part of the axial blastema condense and form a *perichondrium*—a membrane which surrounds growing cartilages. In the 7th and 8th weeks, joints begin to appear in the interchondral discs, the more important before the less important. The manner of formation is the same for all joints: in the periphery of the interchondral disc the mesenchymal cells begin to disappear, giving rise to the synovial space which spreads towards the centre of the developing joint—the central part being the last to be cleared. In the central area of the disc, cartilage cells are formed leading to a temporary union of opposed surfaces (Whillis). The perichondrium is continued from segment to segment over the interchondral discs and thus becomes the basis of the capsular ligament. At first the ends of the cartilages projecting into joint cavities are also covered by an extension of the perichondrium [2]. Peripheral cells of the interchondral disc line the capsule and form the *synovial membrane*, the cells of which, even in the adult, show by their structure that they are cartilaginous in nature. In certain pathological conditions the synovial villi give rise to cartilaginous nodules.

Intra-articular Fibro-cartilages.—In every developing joint fringes of synovial membrane, representing remnants of the interchondral disc (intermediate plate), project into the gap between the articular margins

[35] Haines, R. W., *Jour. Anat.*, 1939, 73, 211 (nature of anconeus muscle).

[36] Zebrowski, P., *Foria Morph.*, 1934, 5, 1 (among Poles the palmaris longus is absent in 18-20%).

[37] For an account of the development of short muscles of digits, see Frazer, J. E., *Manual of Embryology*, 1940.

[38] Seib, G. A., *Amer. Jour. Phys. Anthropol.*, 1934, 19, 229 (psoas parvus absent in 64% of subjects).

[39] Kassatkin, S., *Zeitsch. Anat. Entwickl.*, 1934, 102, 635.

[40] For papers on the supra-condylar process, see Kozlik, F., *Zeitsch. Anat. Entwickl.*, 1934, 102, 772; Adams, Julia L., *Anat. Rec.*, 1934, 58, 44 (suppl.); Gayet, R., *Ann. d'Anat. Path.*, 1937, 14, 607; Dwight, T., *Amer. Jour. Anat.*, 1904, 3, 221.

thigh is extended in the upright posture. Part of it becomes specialized to form the ilio-femoral or Y-shaped ligament. In the knee joint the posterior part of the capsule is strengthened to prevent over-extension. The development of the condyles of the femur towards the popliteal space isolates a posterior part of the capsule which thus comes to lie within the joint and form the crucial ligaments (Fig. 555). The ligamentum teres, the best example of an *intra-articular ligament*, appears in the human foetus as part of the capsule of the joint; in reptiles this foetal form is retained. The round ligament is isolated during the development of the head of the femur, which expands as a wing on each side of the ligamentum teres, and by the fusion of the wings isolates it from the capsule (Fig. 556). The *reflected ligament*, on the under surface

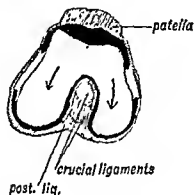


FIG. 555.

FIG. 555. Showing the Origin of the Crucial Ligaments of the Knee.

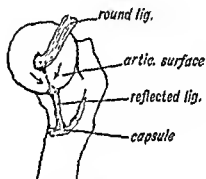


FIG. 556.

FIG. 556. Showing the Origin of the Ligamentum Teres and Reflected Bundle of the Capsular Ligament

of the neck of the femur, is the part of the capsule with which the ligamentum teres was continuous [5].

Knee Joint [6].—In Fig. 557 is given a diagrammatic representation of the posterior aspect of the knee joint as seen in a primitive mammalian type. Three interarticular discs are shown: an internal tibio-femoral, an external tibio-femoral and a fibulo-femoral. When the fibula became excluded from the knee joint, the fibulo-femoral disc, from which fibres of the popliteus took origin, was included in the tendon of that muscle (Carl Fürst). The *popliteus* originally passed from the fibula to the tibia, like the pronator quadratus in the forearm. The upper fibres migrated to the capsule and to the fibulo-femoral disc, and through the disc and its ligaments gained an attachment to the femur. Thus, instead of rotating the tibia on the fibula, the popliteus muscle now rotates the tibia on the femur. Occasionally the cavity of the human knee joint communicates with the superior tibio-fibular joint through

of bones (Fig. 554). In the elbow joint they are present, even in the adult; in the hip and shoulder joint they form the cotyloid and glenoid ligaments. In the knee joint they are much better marked, forming the semilunar cartilages. At the wrist joint the interchondral disc forms the *triangular fibrocartilage*, but here it is possible that certain other elements are included. A nodule of cartilage, which may ossify, is present; within it certain ligaments which united the radius and ulna, and these two bones with the semilunar and cuneiform, have been included (Parsons and Corner). This cartilage is complete in man only; it plays a part in the mechanism of pronation and supination. In the *sterno-clavicular joint* two synovial cavities are formed, one on either side of the inter-

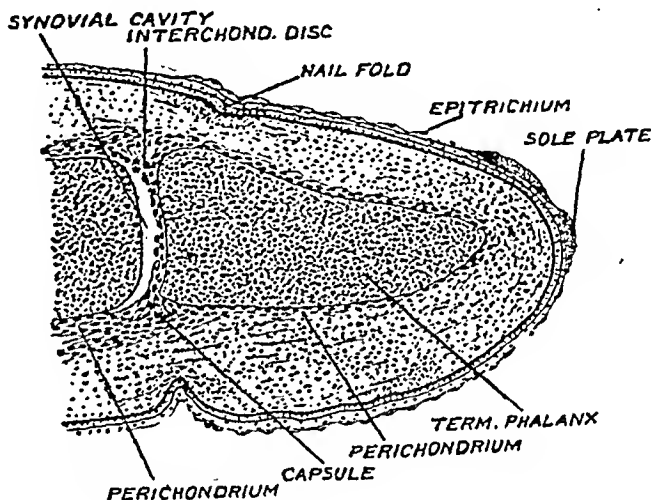


FIG. 554. Sagittal section of Terminal Joint of Finger of Foetus in 10th week of development. (After Nicolas.)

chondral disc. In this case it is only in the higher primates that a complete intra-articular disc is present. Two synovial cavities are also formed in the *temporo-mandibular joint*, the meniscus separating two joints, which are functionally different. The upper is for gliding movements, the lower for hinge-like movements. Intra-articular cartilages not only fill the gaps between incongruous articular surfaces, but, as Dr. MacConaill has demonstrated, serve to maintain the lubricating fluid of the joint as a fine film [3].

Capsular Ligaments.—Certain parts of the capsule of every joint become thickened and specialized according to the strains to which the joint is subjected. Parsons [4] found that it is the middle gleno-humeral ligament of the shoulder joint which becomes enlarged and projects within the joint of pronograde mammals. In man, the coraco-humeral ligament is by far the strongest. The anterior part of the capsule of the hip joint in man has to withstand the strain of the body when the

of cartilage (*a*) such as occur in the growing ends of long bones. In *B*, which depicts a section of the fibrous sheath (perichondrium) of a bone still in its cartilaginous state, the deeper cells (*b*) are seen to be assuming the characters of osteoblasts. They lay down bone under the fibrous

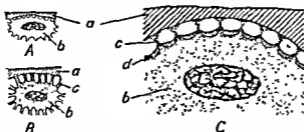


FIG. 558 Stages in the Transformation of a Cartilage Cell into a Bone Cell (Krompecher)

- A.* Cartilage cell (*b*) in contact with a trabecula of calcified cartilage (*a*).
B. The same, now connected with the trabecula by elongated processes (*c*).
C. Greatly magnified part of the cell with bone (*d*) being deposited between the processes and outside the body of the cell.

perichondrium, which thereby becomes periosteum. The more superficial cells (*d, d*) become fibroblasts, fibre-forming cells. Thus we see that fibroblasts, chondroblasts and osteoblasts are modifications of the same type of cell. Under certain circumstances they may return to

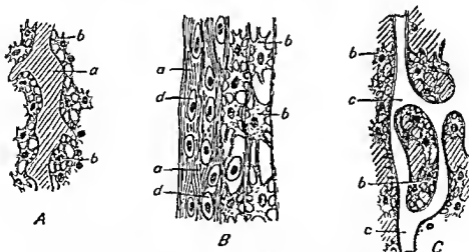


FIG. 559 Illustration of the Three Modes in which Osteoblasts deposit Bone. (After Krompecher)

- A.* Deposition against a column of calcified cartilage (*a*); *b, b*, osteoblasts.
B. Deposition under perichondrium (*a*); *b, b*, chondroblasts becoming osteoblasts.
C. Deposition against the wall of blood channel (*c*); *b, b*, osteoblasts.

their ancestral type, or the one may change into the other. In *C*, the common mode of bone deposition is represented. As may be seen from Fig. 563, the interior of every bone, originally cartilaginous, becomes invaded by an organized vascular system. In the shafts of long bones

the synovial diverticulum beneath the tendon of the popliteus. The upper end of the fibula is already excluded from the knee joint in the 8th week (Fig. 544). There are five separate synovial cavities developed in this joint—one between the patella and femur, two between the femoral condyles and the primitive semilunar cartilages, and two between the cartilages and the upper extremity of the tibia. The five joints become continuous in the 4th month, the crucial and alar ligaments being derived from the primary septa between the cavities [7]. The external semilunar cartilage is circular in form and continuous with the posterior crucial ligament in primates, in which the power of rotation at the knee is highly developed; in man the circular form of the cartilage is lost and it only retains part of its continuity with the posterior crucial ligament [8]. The ligamentum mucosum, which in many mammals

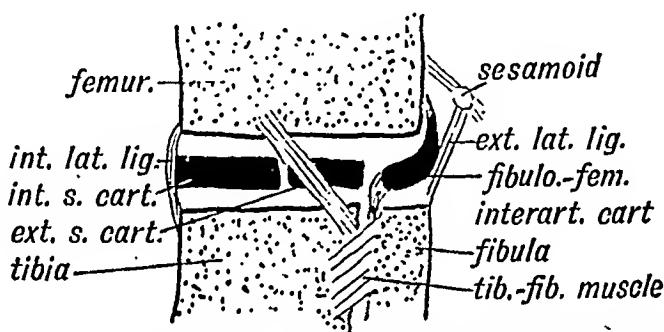


FIG. 557. Scheme of a Primitive Mammalian Knee Joint to show (1) the Articulation of the Fibula with the Femur; (2) the Fibulo-femoral Interarticular Cartilage which becomes included in the Tendon of the Popliteus; (3) the Tibio-fibular Muscle out of which the Popliteus is evolved; (4) the division of the Tibio-femoral Interarticular Cartilage into external and internal Semilunar Cartilages. (Carl Fürst.)

separates the knee joint into three compartments—two condylar and a patellar—is much reduced in man.

If a semilunar cartilage is excised it is replaced by a fibrous body formed from the synovial lining of the capsule [9]. The articular cartilage of joints, like the epidermis of the skin, never ceases to grow and desquamate.

Osteoblasts.—In Fig. 558, stages are shown in the transformation of a cartilage cell into an osteoblast or bone-producing cell. In *A*, a cartilage cell or chondroblast rests against a bar of calcified cartilage (*a*), to which it is connected by numerous short processes. In *B*, these processes (*c*) have become greatly elongated; in *C*, a peripheral part of the cell is shown, greatly magnified. Between its processes a calcified gel has become deposited. With the appearance of this deposit, which is bone, the cartilage cell becomes a bone cell, or osteoblast.

In Fig. 559 osteoblasts are shown at work under three different conditions. In *A* they are beginning to build against a calcified column

is the shaft separating the epiphysial ends which represents a later stage in the evolution of bones.

In the shafts of long bones, to the process of endochondral ossification, another, the ectochondral, is added (Fig. 561, *A, B, C, D*). An endochondral centre is formed as in the tarsal bones, and from this centre the process extends rapidly in every direction. The invading osteoblasts

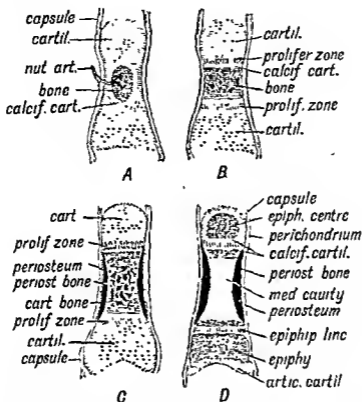


FIG. 561. Ossification of a Long Bone by Endochondral and Ectochondral Ossification. (After Nicolas)

- A. Ossification within the cartilage of the shaft.
- B. Complete ossification of the middle part of the shaft
- C. Formation of bone in the shaft outside the cartilage by osteoblasts lying beneath the perichondrium (now named periosteum).
- D. Complete absorption of the endochondral bone of the shaft; formation of a medullary cavity; appearance of endochondral centres in the epiphyses; formation of the epiphysial lines.

are derived from the deeper cells of the perichondrium (Fig. 559, *B*) perichondral cells become converted, under an undetected influence, into osteoblasts [12]. Some of the osteoblasts, instead of invading the cartilage, form a layer beneath the perichondrium, which surrounds the cartilaginous substance of the bone. The perichondrium now becomes periosteum; the deposit of periosteal (membranous) bone leads to an increase in the thickness of the shaft (Fig. 561, *C*); the extension of the endochondral ossification into the growing cartilaginous ends of

the medullary artery, as it reaches the growing ends, breaks up into a network of fine arterio-venous channels (Fig. 563). In Fig. 559, *C*, osteoblasts are seen to be laying down bone against the wall of such channels. In this way Haversian systems are formed. It is in this manner that bone is laid down under the periosteum of long bones, under the periosteal covering of flat bones, such as those of the skull, and at the epiphysial ends of bones. Further, an osteoblast may change from being an agent concerned in the deposition of bone to one concerned in its absorption (osteoclast).

Ossification of Bones.—The simplest and most primitive manner in which bones pass from the cartilaginous to the osseous stage is seen in the carpus and tarsus (Fig. 560). Bone is deposited within the cartilage by a process of *endochondral ossification*. The various stages in this

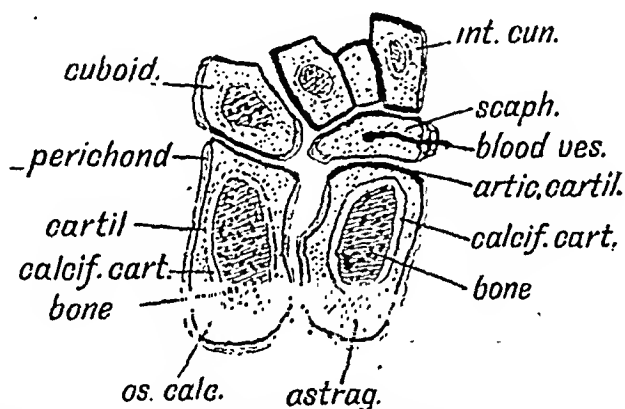


FIG. 560. Section of the Tarsus in the 3rd year of development to show pure Endochondral Formation of Bone.

process may be grouped as follows: (i) calcification of the intercellular matrix in the centre of the bone—a temporary phase in human ossification, but a permanent one in some fishes; (ii) an invasion of vasoformative and osteoblastic cells, which, commencing at a point beneath the perichondrium, reach the middle of the central area of calcification and form a centre of ossification (Fig. 560). The osteoblasts and their accompanying vessels, when the cartilage cells are absorbed, deposit bone in the spaces of the calcified matrix [11]. A section through an ossifying and growing carpal bone shows (i) a centre of ossification; (ii) a surrounding narrow area of calcification; (iii) a peripheral area of actively growing cartilage; (iv) a covering membrane or perichondrium. The processes of growth and ossification cease when the cartilage beneath the perichondrium is completely transformed to bone. Not only are the tarsal and carpal bones formed thus, but so are the epiphysial ends of all long bones. Indeed, we must regard the ends of embryonic long bones as unchanged remnants of an original state; it

diaphysial side of the disc the cartilage cells are growing extremely rapidly; they are arranged in columns; the cells near the middle of the column are undergoing division (Fig. 562). No matter in what plane a cell divides, its progeny moves into its proper place in the vertical rank [14]. The cells as they approach the diaphysial margin undergo a curious change; their nuclei, which eventually disintegrate, appear to occupy empty spaces. These spaces Prof. H. A. Harris found to be filled with glycogen [15]. Osteohlasts invade the spaces; the cartilage between the cell columns undergoes calcification; the bars thus calcified provide a preliminary scaffolding for the invading osteohlasts to build on. Clearly the behaviour of chondrohlasts and of osteohlasts is part of a co-ordinated growth movement. In the disorder of bone-growth known as achondroplasia the cartilage cells are no longer formed in orderly ranks [16].

At maturity the cartilage cells, having ceased to divide, every growth disc becomes permeated with osteoblasts and is finally converted into a plate of dense bone. Such dense plates may be formed at the ends of long bones if growth becomes disturbed from illness or from malnutrition. Later, when growth is resumed, these become incorporated in the shafts, where they appear as transverse lines [17]. The growth disc becomes obliterated earlier in women than in men [18]. Dr. J. W. Pryor found that fusion of the epiphyses with shafts of long bones took place in women between the 14th and 16th years; in men between the 17th and 20th years. The centres of ossification appear earlier in girls than in boys; Dr. Ruth Wallis observed that centres of ossification in the hand—19 in number—were all in existence in girls by the age of 2 years 5 months; in boys they had not all appeared until 5 years of age. The state of ossific centres gives a clue to physiological age as contrasted with age in years. Recent observations have shown that not only should the centres for the distal epiphysis of femur and proximal of tibia be present at birth, but that for the head of the humerus as well. All epiphyses have joined by the 20th year, there are only three exceptions—at the sternal end of the clavicle, along the vertebral border of the scapula, and along the crest of the ilium. The date of union may be delayed from several causes [19].

Nutrient Vessels.—The manner in which nutrient vessels break up to form a mesh work at the growing ends of long bones is illustrated in Fig. 563. In the case of the foetal tibia (*B*) the nutrient artery on entering the medullary cavity is seen to divide into a proximal and a distal branch, each of which ends in a brushwork within the proximal and distal diaphysial discs (*d, l*). The clavicle (*A*) is served by its nutrient artery in much the same way, save that the branch which turns towards

the bone leads to an increase in the length of the shaft. As the periosteal bone is deposited, the endochondral bone within the shaft is absorbed and a medullary cavity is formed, in which *red marrow* begins to appear in the 6th month (Fig. 561, D). The cartilaginous parts of the bone, at each extremity of the shaft, form the epiphyses. When the endochondral centres appear within the epiphyses, a line of growing cartilage

is gradually isolated between them and the endochondral centre of the shaft (Fig. 561, D). At the *epiphysial line* the bone grows in length, the addition being made solely at the shaft or diaphysial side of the line. These growth discs should therefore be named not *epiphysial* but *diaphysial*. Indeed, the addition made by an epiphysis to the length of a long bone is made almost entirely under the articular surface (Payton). By the formation of epiphyses at the ends of long bones, the growing line of cartilage is sheltered from the friction and stress to which it would be exposed if situated on the articular ends of the bones. All the cartilage of a bone, except that on the articular surfaces, is ossified when the body is fully grown. In the growth of a long bone, such as the humerus, the proximal and distal diaphysial lines take an unequal share [13]. Digby found that while the proximal line added 4 parts to the length of the humerus the distal line contributed only 1 part. By feeding pigs on madder Dr. C. G. Payton succeeded in demonstrating the rates at which growth takes place at both proximal and distal ends of the shafts of long bones. The most rapidly growing of all the epiphysial lines of the body is that at the distal end of the femur; it is therefore the most liable to be affected in rickets (H. A. Harris). On the other hand the disc at the proximal end of the humerus

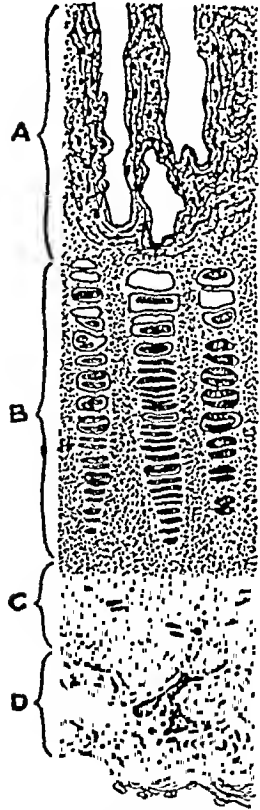


FIG. 562. Section of the Growth Disc of a Human Long Bone. (After Prof. Derry.) A, Zone of bone of diaphysis, just laid down; B, zone of cartilaginous proliferation for growth of diaphysis; C, cartilage zone of epiphysis; D, bone of epiphysis just formed.

is the last of those of long bones to "close down" (19th to 21st year). The chief nutrient canal of a long bone points to the centre at which endochondral ossification commenced in the shaft.

Diaphysial or Growth Discs.—In Fig. 562 is given a diagrammatic representation of an "epiphysial line" or growth disc from a human long bone approaching maturity. The cartilage cells along the *epiphysial* margin are arranged irregularly; epiphysial osteoblasts are invading the cartilage and laying down bone only to a slight extent. On the

diaphysial side of the disc the cartilage cells are growing extremely rapidly; they are arranged in columns; the cells near the middle of the column are undergoing division (Fig. 562). No matter in what plane a cell divides, its progeny moves into its proper place in the vertical rank [14]. The cells as they approach the diaphysial margin undergo a curious change; their nuclei, which eventually disintegrate, appear to occupy empty spaces. These spaces Prof. H. A. Harris found to be filled with glycogen [15]. Osteoblasts invade the spaces; the cartilage between the cell columns undergoes calcification; the bars thus calcified provide a preliminary scaffolding for the invading osteoblasts to build on. Clearly the behaviour of chondroblasts and of osteoblasts is part of a co-ordinated growth movement. In the disorder of bone-growth known as achondroplasia the cartilage cells are no longer formed in orderly ranks [16].

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the acromial end does not terminate in a distinct brush of vessels, for at that end there is no epiphysial disc. The nutrient arteries are the chief source of supply to long bones until the 2nd year, when periosteal vessels take over the nourishment of all but the interior parts.

Remodelling [21].—In Fig. 563, *C*, the distal end of a femur illustrates a failure in the process of remodelling. The growth disc of a long bone is always wider than the more proximal part of its shaft. The adult width of the disc in *C* is indicated by the line *a-a*; its width at the 13th year is indicated by the line *a'-a'*. In the normal process of remodelling,

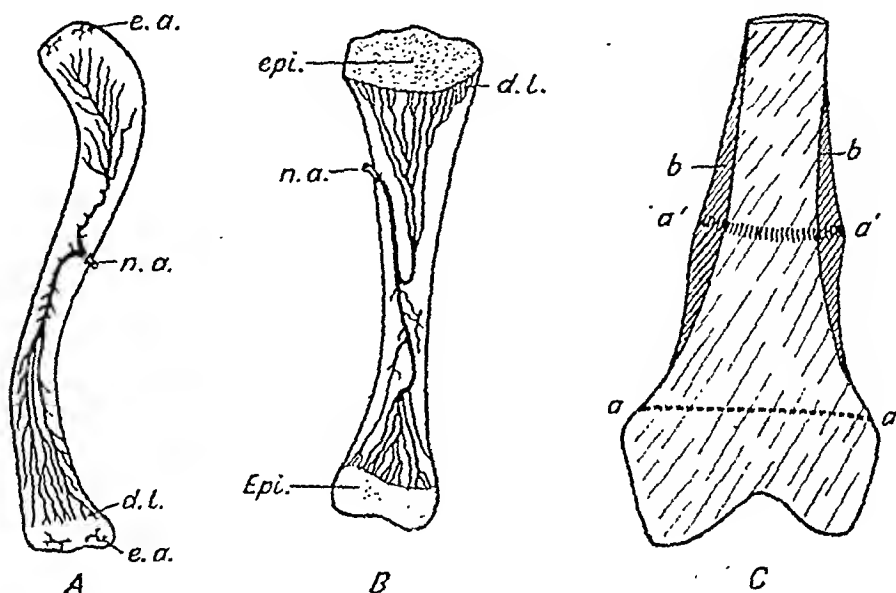


FIG. 563.

- A.* A Clavicle of a newly born Child with its nutrient arteries injected. (Anseroff.)
B. Tibia of a 7th-month foetus with its nutrient artery injected. (Anseroff.) *n.a.*, nutrient artery; *d.l.*, diaphysial growth line; *e.a.*, epiphysial arteries; *Epi.*, cartilaginous epiphysis.
C. Femur showing a cylindrical thickening of the distal part of its shaft due to a failure of the remodelling process. (After Suk.) *a-a*, width of diaphysial disc at maturity; *a'-a'*, width in adolescence; *b, b*, bone which should have been absorbed in the process of remodelling.

which follows in the rear of the growing disc, the peripheral bone (*b, b*) is absorbed and the diameters reduced to the size shown in the illustration. John Hunter was the first to realize and demonstrate the extent to which bones are remodelled as they grow. Prof. Brash has shown the extent to which even the tabular bones of the skull are reshaped as they grow [21]. In the disorder of growth known as diaphysial aclasis, there is an extensive failure in the process of remodelling [22].

Control of Osteoblasts [23].—With the discovery of hormones at the beginning of the present century, together with a more accurate knowledge of growth disorders, such as acromegaly, achondroplasia, etc., it became apparent that bone formation was influenced by substances formed in

glands of internal secretion. In the third decade of this century three discoveries were made which threw new light on bone formation: (i) The discovery that the amount of calcium in circulation was regulated by the action of the parathyroids: adenomatous enlargement of the parathyroid led to absorption of certain areas of bone. (ii) The discovery by Dr. R. Robison, of the Lister Institute, London, that the deposition of calcium salts to form bone is regulated by an enzyme—*phosphatase* [24]. Phosphatase is present in the plasma of the blood and is formed by various kinds of cells—including osteoblasts and particularly by ripe distended cartilage cells. Prof. Harris infers from the presence of glycogen in enlarged cartilage cells at the sites of ossification that such cells also produce phosphatase. (iii) The discovery that embryonic bones can be kept alive and studied by the same methods as are employed by bacteriologists in the study of micro-organisms [25]. By using such methods Dr. Honor Fell has greatly enlarged our knowledge of the life-histories of cartilage cells and of bone cells. And (iv) the recognition that a due proportion of vitamins and of mineral salts must be present in a child's diet if its ossification is to proceed normally.

For some years surgeons have recognized that a transplant of dead bone serves quite as well as a living one to induce a formation of new bone. One must infer that in bone, be it dead or alive, there is a substance which serves as an invocator in calling out the bone-forming competence of living cartilage cells, or connective tissue cells, with which a transplant is brought in contact. Cartilage also contains such an agent. When an extract made from the epiphysial ends of the bones of newly born rabbits is injected into the thigh muscles of adult rabbits, true bone is formed at the site of injection (Lacroix).

Nature of Epiphyses.—Epiphyses are of three kinds [26]: (i) pressure epiphyses, forming the articular extremities of long bones (Fig. 564, B); (ii) traction epiphyses, which form processes for the insertion of muscles (Fig. 564, B); (iii) atavistic epiphyses, formed by the union of an element which formerly existed as a separate bone (Fig. 564, A).

The upper extremity of the femur affords typical examples of pressure and traction epiphyses. By extension of the ossification of the shaft within the cartilage of the upper extremity of the femur, the pressure and traction epiphyses become widely separated to form the head and trochanters. *Pressure epiphyses* are the first to ossify, their centres appearing in the order of their functional importance; they are always fitted to the shaft by a species of dovetailing to withstand dislocating forces. The upper extremity of the shaft of the humerus projects as a three-sided pyramid within the epiphyses; the lower end of the shaft of the femur is fitted within its lower epiphysis by a number of projections not well

marked in the human bone but pronounced in those animals which maintain the knee in a flexed position. Epiphyses are mammalian characters; yet their rudiments are to be seen in reptilia [27].

The great trochanter is the *traction epiphysis* of the gluteus medius and minimus; the small trochanter, of the psoas and iliacus; the 3rd trochanter, in which a centre appears in the 20th year, that of the gluteus maximus. In the 5th foetal month a trough-like depression appears at the insertion of the gluteus maximus. A ridge arises at the lateral border of the trough and usually grows over and obliterates the depression. The 3rd trochanter arises at the upper or proximal end of the trough; it is more frequently to be found in the femur of man than in that of any other of the primates [28]. The epiphysis of the great

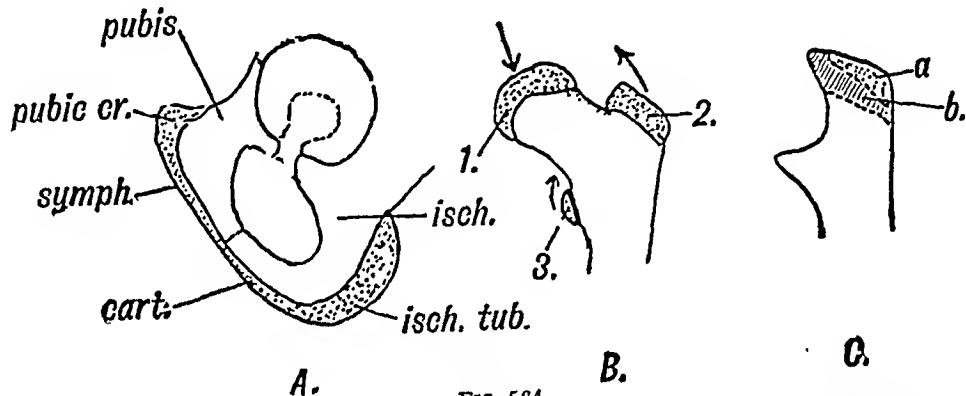


FIG. 504.

- A. The Epiphysal Cartilage of the Pubis and Ischium, which arises from the median cartilage of the pelvic girdle. (Parsons.)
 B. Traction and Pressure Epiphyses on the upper extremity of the Femur.
 C. The Epiphyses of the Olecranon: *a*, the usual epiphysis; *b*, occasional epiphysis; both *a* and *b* may be present. (Fawcett.)

trochanter of the rabbit continues to develop normally although the insertions of the gluteal muscles have been detached (Appleton) [29].

As examples of *atavistic epiphyses*, Parsons cited the following: those of the ischium and pubis (Fig. 504, A) from the median pelvic bar (Figs. 516, 564); the coracoid process; the epiphysis on the os calcis, the scale-like epiphysis of the olecranon (Fig. 504, C). The internal and external epicondyles of the humerus may be derived from *sesamoid ossifications*, such as are now seen in the patella, in the tendons of the popliteus, outer head of gastrocnemius (occasional), peroneus longus, tibialis posticus and at the metacarpo-phalangeal joints of the thumb and great toe [30]. The *patella* is usually regarded as a sesamoid, but Mlle. Bertha Vriese collected evidence to show that it is really a true morphological skeletal element [31].

The patella, which begins to be developed in the deep fibres of the tendon of the quadriceps muscle in the 7th week (Walmsley), is ossified

from one or sometimes two centres, which appear in the 2nd year. Occasionally the patella is bipartite [32].

Blood-Supply of Epiphyses [33].—In the 5th month of foetal life vessels penetrate at many points on the surface of epiphyses, all save their articular areas. Such vessels arise as ingrowths from the vascular perichondrium (Hurrell); they represent local submergenees of the perichondrium (Haines)—both interpretations may be valid.

Aberrant Epiphyses [34].—The metacarpal bone of the thumb, although it is in the same series as other metacarpals, yet, as it serves as a phalanx, ossifies in the phalangeal way, namely, with only a proximal epiphysis

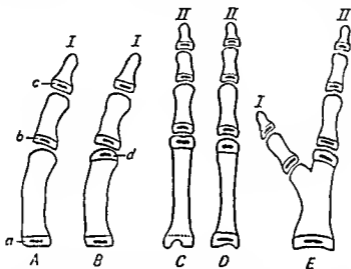


FIG 565.

- A. Bones of the thumb with normal proximal epiphyses (a, b, c).
- B. Bones of the thumb, the metacarpal having a distal as well as a proximal epiphysis.
- C. Bones of the 2nd digit with the usual epiphyses.
- D. The same, save that the metacarpal has a proximal as well as a distal epiphysis.
- E. A case where the 1st and 2nd metacarpals are conjoined, there being a common proximal epiphysis, but only the 2nd metacarpal has a distal epiphysis.

(Fig 565, A). Like other metacarpals, it may also have a distal epiphysis and still retain the proximal one (Fig. 565, B). The 2nd and 5th metacarpals—and the same is true of the corresponding metatarsals—have occasionally a proximal epiphysis (D). It is the distal ends of the same metacarpals that may be provided with sesamoids (see p. 629). In cases where the 1st and 2nd metacarpals are conjoined, as in “claw hand,” there may be a common proximal epiphysis (E), but only the 2nd metacarpal has a distal epiphysis. If digits undergo reduction of development, as in the three outer toes of the human foot, the imperfection is centred in the middle phalanx; it may remain unseparated from the terminal phalanx. This also occurs in cases of brachydactyly [33].

Lines of Pressure and Tension of Bones.—The trabeculae in which the

marked in the human bone but pronounced in those animals which maintain the knee in a flexed position. Epiphyses are mammalian characters; yet their rudiments are to be seen in reptilia [27].

The great trochanter is the *traction epiphysis* of the gluteus medius and minimus; the small trochanter, of the psoas and iliacus; the 3rd trochanter, in which a centre appears in the 20th year, that of the gluteus maximus. In the 5th foetal month a trough-like depression appears at the insertion of the gluteus maximus. A ridge arises at the lateral border of the trough and usually grows over and obliterates the depression. The 3rd trochanter arises at the upper or proximal end of the trough; it is more frequently to be found in the femur of man than in that of any other of the primates [28]. The epiphysis of the great

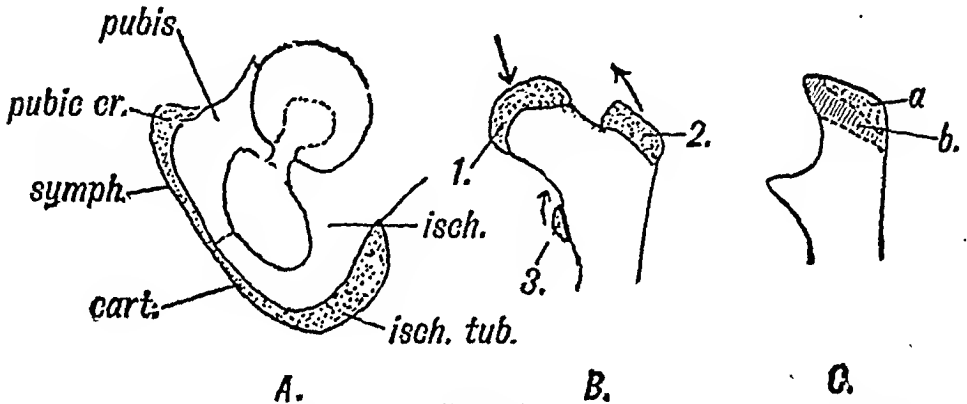


FIG. 564.

- A. The Epiphysial Cartilage of the Pubis and Ischium, which arises from the median cartilage of the pelvic girdle. (Parsons.)
 B. Traction and Pressure Epiphyses on the upper extremity of the Femur.
 C. The Epiphyses of the Olecranon: *a*, the usual epiphysis; *b*, occasional epiphysis; both *a* and *b* may be present. (Fawcett.)

trochanter of the rabbit continues to develop normally although the insertions of the gluteal muscles have been detached (Appleton) [29].

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The patella, which begins to be developed in the deep fibres of the tendon of the quadriceps muscle in the 7th week (Walmsley), is ossified

[2] In some joints, the temporo-mandibular for example, the lining of embryonic perichondrium persists (see Charles, S. W., note [32], Chapter XIII).

[3] MacConaill, M. A., *Jour. Anat.*, 1932, 66, 210; for origin and nature of synovial fluid, see Davies, D. V., *ibid.*, 1943, 77, 160; 1944, 78, 68; 1945, 79, 66; *Lancet*, 1946, 2, 815 (gives recent literature); Kling, D. H., *Synovial Membrane and Fluid*, 1939.

[4] Parsons, F. G., *Jour. Anat.*, 1900, 34, 301; Keith, Sir A., *ibid.*, 1894, 28, 149 (ligaments in Primates).

[5] Walmsley, T., *Jour. Anat.*, 1917, 51, 61.

[6] Walmsley, R., see note [1]; Haines, R. W., see note [1].

[7] Bardeen, C. R., see note [4], Chapter XXIX.

[8] Harris, H. A., *Lancet*, 1934, 1, 1114; Charles, C. M., *Anat. Rec.*, 1935, 63, 355 (observations on 1433 knee-joints).

[9] Walmsley, R., and Bruce, J., *Jour. Anat.*, 1938, 72, 260; *Brit. Jour. Surg.*, 1937, 25, 17. For repair of intra-articular cartilages, Elliott, H. C., *Amer. Jour. Anat.*, 1936, 58, 127; Bennett and Others, *Amer. Jour. Path.*, 1932, 8, 499 (repair of cartilages).

[10] For the manner in which bone is developed and the conditions under which it is formed, see Harris, H. A., *Bone Growth in Health and Disease*, 1933; Murray, P. D. F., *Bones: A Study of Development and Structure of the Vertebrate Skeleton*, 1933.

148 (bone grafts as evocators); Pritchard, J. J., *Jour. Anat.*, 1947, 80, 225 (splenic and testicular grafts as osteogenic stimulants); Crawford, G. N. C., *Jour. Anat.*, 1940, 74, 284 (evolution of Haversian pattern); Gluckmann, A., *ibid.*, 1942, 76, 231 (influence of stress on developing bone).

[11] I have written as if osteoblasts were carried in from the perichondrium, which was, and is, the view commonly accepted. It becomes more probable that osteoblasts arise from the cartilage cells of the calcified centre of an epiphysis and that it is the calcification which attracts perichondrial vessels.

[12] The connective tissue of certain structures are more easily "induced" to form bone than that of others, see Carey, E. J., *Amer. Jour. Anat.*, 1936, 59, 89; Reegan and Wilkins, *Jour. Lab. Clin. Med.*, 1934, 20, 250; Toro, E., *Anat. Anz.*, 1935, 80, 285; Keith, Sir A., *Proc. Roy. Soc. Med.*, 1928, 21, 301 (surg. sect.).

[13] For comparative growth at proximal and distal ends of long bones, see Payton, C. G., *Jour. Anat.*, 1933, 67, 371; Digby, K., *ibid.*, 1916, 50, 186; Krogman, W. M., *Amer. Anthropol.*, 1935, 37, 92 (growth of long bones in anthropoids).

[14] For growth of cartilage in diaphysial discs, see Dodds, C. S., *Anat. Rec.*, 1930, 46, 385; Ham, A. W., *ibid.*, 1931, 51, 125; see also Harris, H. A., and Murray, P. D. F., note [10].

[15] *Nature*, 1932, 130, 996; Fell and Robison, *ibid.*, 1933, 131, 62; Borghese, E., *Zeitsch. Zellforsch. Mik. Anat.*, 1936, 25, 622.

[16] For growth of cartilage in Achondroplasia, see Harris, H. A., note [10]; Fell and Landauer, *Proc. Roy. Soc.*, 1935, 118 (B), 133; Keith, Sir A., *Jour. Anat.*, 1913, 47, 189; Mortimer, H., *Radiology*, 1937, 28, 5.

[17] Harris, H. A., note [10]; Selye, H., *Jour. Anat.*, 1934, 68, 289; Cohen and Friedman, *Jour. Allergy*, 1937, 9, 54.

[18] For dates at which centres of ossification appear and at which epiphyses

bony matter is deposited by the osteoblasts, are arranged so as to withstand the forces to which the body is subjected, thus exemplifying Wolff's law [35]. When a bone, such as the astragalus, rib or neck of the femur, is laid open by a section, the trabeculae appear to form straight lines or septa, which converge and meet at various angles; when, however, such bones are examined stereoscopically with X-rays, the trabeculae are seen to be arranged in a double spiral—one system twisting from right to left, the other from left to right (Haughton and Dixon) [36]. By this means the greatest strength is obtained with the least expenditure of material.

Bones serve also as storehouses of calcium for the use of the bodily economy. When bone is absorbed, as in functional atrophy, it is the transverse or tension lamellae which undergo reduction first (Harris).

Morphogenesis of Long Bones [37].—Prof. Appleton produced an alteration of torsion in the femora of growing rabbits by section of the muscles which act as internal rotators. If a limb is deprived of its nerve supply, its bones attain their normal length, but are slender and destitute of muscular markings (Tower). If fibrous tissue is permanently compressed, it assumes the texture of cartilage (Krompecher); if a segment of the rectus abdominis is treated in a similar way, it becomes bony (Carey). With the assumption of the quadrupedal gait, the vertebrate fore-limb underwent rotation so that the elbow became directed backwards, while in the hind limb the knee was turned in front. Forward propulsion in the fore-limb was obtained at the elbow, while in the hind-limb this was obtained at the ankle joint. Thus, in a functional sense, the heel corresponds to the olecranon (Martin). Flattening of the tibia from side to side (platycnemia) and flattening of the proximal shaft of the femur (platymeria), conditions which prevailed amongst the ancient inhabitants of Britain, still remain unexplained. These features of the tibia and femur do not appear to be due to peculiarities in gait, for the late Dr. Dudley Buxton found that there were corresponding changes in the bones of the upper extremity. As the human brain underwent its evolutionary elaboration there appears to have been a corresponding elaboration in the architecture of the human skeleton (Wright).

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metacarpals); Monteiro and Carvalho, *hydactyly*, 1932, 50, 435; Stacey, R. S., *Jour. Anat.*, 1932, 50, 435; MacArthur and McCullough, *Human Biol.*, 1932, 4, 179 (apical dystrophy). For union of digits, see Pryor, J. W., *Amer. Jour. Anat.*, 1936, 58, 87; Teixeira, C., *Trabalhos Soc. Portug. Anthropol.*, 1935, 7, 241; Nicholson, G. W., *Guys Hosp. Rep.*, 1937, 87, 46 (hand from a sacro-coccygeal tumour).

[35] See references to Harris and to Murray, note [10]; see also Keith, Sir A., *Minders of the Maimed*, 1919.

[36] Dixon, A. F., *Jour. Anat.*, 1910, 44, 223.

[37] Appleton, A. B., *Lancet*, 1934, 1, 451; Stewart, D., *Jour. Anat.*, 1939, 73, 195 (effects of gait); Tower, Sarah S., *Jour. Comp. Neur.*, 1937, 67, 241 (effects of neurotomy on bone form); Hurrell, D. J., *Jour. Anat.*, 1938, 72, 54 (nerves to bones); Krompecher, S., *Anat. Anz.*, 1938, 85, 229 (suppl.); Martin, C. P., *Jour. Anat.*, 1934, 68, 510; Buxton, L. H. Dudley, *ibid.*, 1939, 73, 31; Wright, R. D., *ibid.*, 1935, 69, 89; Amprino and Cattaneo, *Zeitschr. Anat. Entwickl.*, 1937, 107, 680 (muscular insertions and markings); see also Gluckmann, A., note [10].

fuse, see Todd, T. W., *Atlas of Skeletal Maturation*, 1936 (the summary of a life's work); Basu, S. Kumar, *Indian Med. Rec.*, 1938, 58, 97 (in natives of India); Sidhom and Derry, *Jour. Anat.*, 1931, 65, 196, (in Egyptians); Flecker, H., *ibid.*, 1933, 67, 118; Scammon, R. E., *Anat. Rec.*, 1927, 35, 241 (summarizes literature on ossification); Wallis, Ruth, *Univ. of Iowa Studies*, 1931, 5, 1; Barrett, J. H., *Jour. Anat.*, 1936, 70, 432 (among Burmese); Pryor, J. W., *Amer. Jour. Anat.*, 1936, 59, 409 (in twins, like and unlike); Paterson, R. S., *Jour. Anat.*, 1930, 64, 28; Schultz, A. H., *Contrib. Emb.*, 1937, 26, 73 (in apes and monkeys).

[19] Todd, Wharton and Todd, *Amer. Jour. Anat.*, 1934, 55, 97; 1938, 63, 37 (delay due to thyroid deficiency); Cave, A. J. E., *Jour. Anat.*, 1938, 72, 318 (delay in eunuchs); see also references under note [16].

[20] For recent papers on nutrient arteries, see Anseroff, N. J., *Zeitsch. Anat. Entwickl.*, 1934, 103, 793; Payton, C. G., *Jour. Anat.*, 1934, 68, 500.

[21] For remodelling of growing bones, see Hunter, John, *Collected Works*, 1837, vol. IV, 315; Brash, J. C., note [10]; Ingalls and Grossberg, *Amer. Jour. Phys. Anthropol.*, 1932, 16, 475; Grünberg, H., *Jour. Anat.*, 1937, 71, 237 (a lethal disease in mice attended by an absence of remodelling); Barnicot, N. A., *Amer. Jour. Anat.*, 1941, 68, 498; *Jour. Anat.*, 1945, 79, 83 (further observations on the same disorder of mice); Robinson and Best, *Anat. Rec.*, 1943, 59, 283 (exostosis caused by feeding rats with Lathyrus peas); Dijkstra, O. H., *Ann. d'Anat. Path.*, 1935, 12, 131 (marble bones).

[22] Keith, Sir A., *Jour. Anat.*, 1920, 54, 101 (diaphysial aclasis).

[23] See references given in notes [10], [12], [16]. See also Ray, Evans and Becks, *Anat. Rec.*, 1942, 82, 67 (influence of pituitary); Keith, Sir A., *Lancet*, 1911, 1, 993 (acromegaly); 1913, 1, 305 (progeria).

[24] Robison, R., *Biochem. Jour.*, 1923, 17, 286; Fell and Robison, *ibid.*, 1929, 23, 767; 1930, 24, 1905; 1934, 28, 2243.

[25] For summary of the application of cultural methods to bone growth, see Levi, G., *Ergeb. Anat. Entwickl.*, 1934, 31, 125. Strangeways and Fell began to explant limb-buds of chick embryos in 1925.

[26] On epiphyses, see Parsons, F. G., *Jour. Anat.*, 1903, 37, 315; 1904, 38, 248; 1908, 42, 388; Haines, R. Wheeler, *ibid.*, 1938, 72, 323; 1939, 73, 362; 1940, 74, 90; 1941, 75, 282.

[27] Dr. Wheeler Haines has traced the evolution of epiphyses in the vertebrate phylum (see references in preceding note). He finds that what is peculiar to mammals is not that their epiphyses have separate centres of ossification but that their growth discs have become arranged in a transverse plane.

[28] Hrdlicka, A., *Amer. Jour. Phys. Anthropol.*, 1938, 23, 127; Apostolakis, G., *L'Anthropologie*, 1931, 41, 501 (third trochanter occurs in 28% of subjects).

[29] Appleton, A. B., *Proc. Anat. Soc.*, 1925, p. 30.

[30] Pearson and Davin, *Biometrika*, 1921, 13, 133, 356.

[31] de Vriese, Bertha, *Bull. l'Acad. Sc. Belg.*, 1909, March 27; for development of patella, see Walmsley, R., note [1].

[32] For anomalies of patella, see George Ruggles, *Brit. Jour. Surg.*, 1935, 22, 555; Oetteking, B., *Anat. Rec.*, 1922, 23, 269.

[33] For development of vessels in epiphyses, see Haines, R. W., *Jour. Anat.*, 1934, 68, 45; 1937, 71, 471 (to patella); Hurrell, D. J., *ibid.*, 1936, 69, 47.

[34] For variations in ossification of digits, see Weddell, G., *Jour. Anat.*, 1939, 73, 360 (80% of children have both proximal and distal epiphyses to metacarpal of thumb); Posener and Others, *ibid.*, 1940, 74, 76 (pseudo-epiphyses of

fine hairs or lanugo. This is also the condition in the human foetus at a corresponding period; in man, although the foetal crop of lanugo is succeeded by a general outgrowth of fully developed hair, yet we may regard the human condition as representing an arrest of hair development at a stage seen in foetal apes. Man has come by his hairlessness, as by many of his other characteristics, by retaining to adult life features which appear only in the developmental life of great anthropoids [2]. The human skin is also more sensitive and more richly supplied with sensory nerves than is the case in other primates. It was the opinion of the late Sir G. Elliot-Smith that the rich sensory supply to the skin must have been a factor in bringing about the large size of the human brain. Perhaps it is better to regard brain and skin development as correlated processes.

There are on record a number of cases of men and women in whom the whole surface of the body was coated with a close covering of hair. The development of hair on the face is certainly regulated by a secretion derived from the sexual glands, for in eunuchs the beard is never developed. It is also well known that the pituitary, adrenal and thyroid have a direct influence on the development and growth of hair. Desquamation from the epidermis begins in the 3rd month of foetal life and never ceases until death. In a certain disease of foetal life, named *Ichthyosis*, desquamation does not take place; the unshed epidermis forms cracked cakes on the surface of the child at birth. Hairlessness characterizes certain breeds of dogs and mice [3].

Development of the Skin [4].—Considerable assistance in the understanding of the diseases to which the skin is liable and of the nature of the growths which arise from the epidermis, such as corns, bunions and cancer, is to be obtained by studying the manner in which the skin is developed. At first the human embryo is covered by a single layer of epithelium (*epiblast* or *ectoderm*), as is the case in the adult amphioxus. By the end of the 1st month there are two layers, the lower representing the *germinal* or basal layer; the upper the *epitrichium*, so named because it was supposed that hairs are developed beneath it, and when they grow out in the 3rd month this surface layer of flat epithelium was shed. This evanescent foetal layer is also known as the periderm. During the 2nd month growth activity is more marked in the mesoderm of the cutis than in the ectoderm; on the 3rd month this incidence is reversed (Steiner).

In the 3rd month we find development processes in full activity in the skin; three strata are recognizable in the epidermis—all derived from the single germinal layer. These are: (i) a basal layer—a single stratum of cubical or columnar cells, representing the primitive germinal epithe-

CHAPTER XXXII

SKIN AND ITS APPENDAGES

Stages in the Evolution of the Skin.—We have already seen that the structures which are developed in the human embryo can be best explained by supposing that at one stage of evolution the ancestry of mammals lived and breathed in water. The skin of the human embryo until the end of the 2nd month of development is translucent, and has many points in common with that of the lowest gill-bearing vertebrates. It then consists of two layers—a deep or germinal, consisting of cubical epithelium, and a superficial, made up of flattened cells (Fig. 567, *A*). In the 3rd month this superficial layer, known as the *epitrichium* or

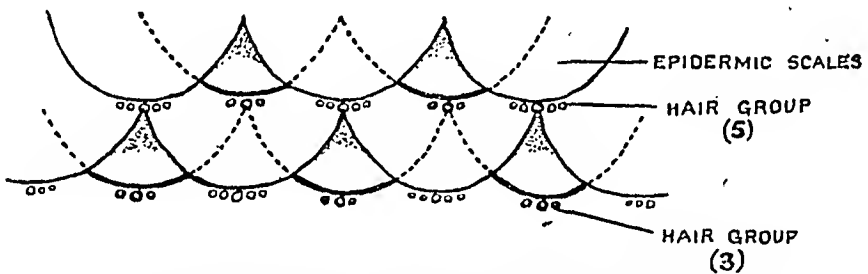


FIG. 566. Showing the Arrangement of Hair Groups in the Human Foetus and their Relationship to Hypothetical Dermal Scales. (Stöhr.)

periderm, becomes horny in nature, recalling a stage which represents the evolution into a terrestrial form of life. The appendages of the skin—its hair and glands—appear later; they seem to be modifications of glandular and sensory structures seen in the soft skin of amphibia. The hairs are developed in groups and lines [1]. Their arrangement can be accounted for by supposing that the skin of primitive mammals was covered by scales and that the hairs sprouted out in groups at their tessellated junctions, as in certain living edentates (see Fig. 566). The human hairs are arranged in irregular series, but in most instances only the chief hair of a group is developed. In a late period of foetal life, however, the chief hair has one or two subsidiary hairs planted on either side of it—making one of a group of three or five hairs.

The skin of man, compared to the other primates, is comparatively hairless. We must regard his nudity as a lately acquired character. At the 7th month of foetal life the chimpanzee and gorilla have hair only on the scalp, eyebrows and lips; the rest of the body is nude, except for

subsequently subdivided into papillae. The down-growing nature of the ectodermal (epidermal) cells which is here exemplified is of the greatest clinical importance. The enamel organs, we have seen, arose by a species of downgrowth of the epidermis; so do hairs, sweat glands and sebaceous follicles. Prolonged pressure and friction weld the corneous cells into a solid plate, such as the callosities seen on the palms of manual labourers. Normal desquamation is arrested; the cells produced in the deeper layers, unable to grow to the surface, grow inwards and produce corns. In cancer, the epithelial cells of the skin renew their youth and invade the dermis and deeper tissues.

Sweat glands begin to arise as buds from the ectodermal troughs in the 4th month foetus (Fig. 567, B). Their ducts open on the surface of the skin in lines or rows corresponding to the primary epidermal furrows. In the 5th month the epidermis round their mouths is raised into ridges, and it is these ridges which give rise to the papillary patterns on the balls of the fingers and elevations of the palm. It will be



FIG. 568. The more common patterns formed by the Dermal Papillae on the Tips of the Fingers.

A, the loop pattern. B, the triangle pattern. C, the whorl pattern.

thus seen that the epidermal ridges correspond not to the lines of dermal papillae, but to the furrows of epidermis lying between the papillae.

The papillary lines on the palms and fingers are richly supplied by nerves and serve as organs of touch; they also give security of grasp (Hepburn). They are arranged in most variable patterns, but the prevailing types in man are those arranged as loops, spirals or whorls (Fig. 568). These are also the patterns found on the hands and feet of anthropoid apes [7]. So much does each pattern vary and so variable is the sequence of the patterns on the pulps of the digits, that no two people show exactly the same patterns occurring in the same order counting from thumb to little finger in both hands. Hence the impress of the ten finger-tips has been successfully used in the identification of criminals. The patterns on the left hand do not represent a mirror-image of those of the opposite or right hand; certain combinations are characteristic of the right hand, others of the left. In people who are congenitally left-handed the combinations in the two hands are more alike than is the case in right-handed people (Newman).

lium (Fig. 567, *B*); (ii) an intermediate or mucous stratum, several cells deep; (iii) a heaped-up superficial or corneous stratum, representing the protecting but perishing superficial covering of the skin. At the same time the opening phases in the development of hair follicles, sebaceous and sweat glands and of skin ridges and papillae are to be detected. In the 5th month the *stratum lucidum* becomes differentiated between the mucous and corneous strata.

The epidermis rests at first on undifferentiated *mesoderm*, consisting of small round cells closely imbedded in a mucoïd matrix. This is the normal structure of undifferentiated *mesoderm*. The superficial mesodermal cells become condensed beneath the epidermis to form a corium towards the end of the 2nd month; an areolar or subcutaneous stratum of tissue is differentiated at the same time. Connective tissue fibrils begin to develop in the mucoïd substance (gel) immediately surrounding the mesodermal cells and by the 5th month the mucoïd substance has

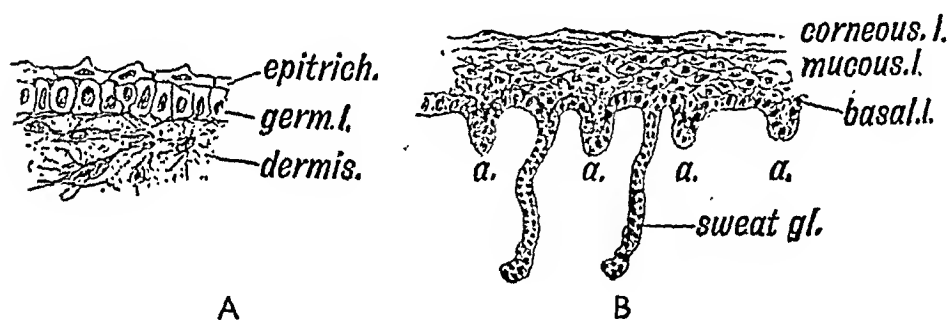


FIG. 567.

- A. Diagrammatic section of the Skin at the commencement of the 2nd month.
 B. Diagrammatic section of the Skin at the commencement of the 5th month.
 a. a. a. Infoldings of the epidermis between the primary ridges.

almost disappeared; but even in adult life, when the thyroid body is diseased or removed, a mucoïd substance may reappear, and a condition resembling the foetal state be thus produced. In the mucous membranes of the lips, anus and vulva, the superficial layer of epithelium does not become cornified.

Formation of Dermal Papillae [5].—Up to the end of the 3rd month the epidermis is easily detached from the corium as a flat membrane, but early in the 4th month they become more closely united by ridges of epidermis becoming folded within corresponding furrows on the corium. About the 4th month, the dermal papillae, which are grouped in lines and ridges, as is well seen in the palm, are formed in the following manner:

Long, linear furrows of epidermis grow down into the dermis (corium) and divide its surface into narrow ridges (Fig. 567, *B*). These ridges are

skin of reptalia (Gegenhaur). These touch hodies are composed of epithelial cells, having the same shape and arrangement as those which form the taste buds in the circumvallate papillae of the human tongue. The cells which cap the hair papilla evidently represent the primary sensory cells of the touch hodies; they are situated in line, and continuous with the basal or germinal layer of the skin. The primary function of the hairs as touch organs is seen in the vibrissae round the mouths of carnivora. Friedenthal has found that certain of the hair-roots in the lips and eyebrows of the human foetus develop the same large sensory

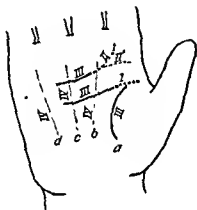


FIG 570

FIG 570. Palm of the Hand of a Human Foetus showing the order in which the crease lines appear. The first, *I*, is present at 8 weeks, *II*, at 9 weeks, *III*, at 12 weeks, and *IV* at 14 weeks (Würth)

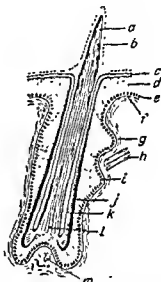


FIG 571.

FIG 571. A diagram to show the Relation of the Sheaths of a developing Hair-root to the Strata of the Epidermis (After Jordan and Kindred)

a, apex of hair-raising periderm (*b*); *c*, combined stratum corneum and stratum lucidum, which form the sheath of Huxley (*A*), and of Henle (*J*); *d*, stratum granulosum (mucosum), *e*, stratum germinativum; *f*, cutis; *h*, anlage of arrector pila; *g*, anlage of new hair-root, *i*, hair bulb; *m*, hair papilla

bulbs as are found in the roots of the vibrissae of lower mammals, but in man their appearance is transient. Lower primates have a tuft of vibrissae placed amongst the hairs of the wrist. It is situated towards the ulnar border of the flexor surface, and serves as a special touch organ. Dr. A. H. Schultz found a vestige of the wrist vibrissae in the human foetus [8].

The first stage in the development of a hair is the ingrowth of epidermis as a solid bud, which pushes in front of it the dermis to form the papilla on which the hair grows (Fig. 572). All strata of the epidermis, save the periderm (epitrichium), are carried inwards to form the hair sheath and hair root. Three stages in the development of a hair follicle are

These epidermal patterns are formed on elevations which appear on the human hand and foot at the end of the 2nd month, and which certainly correspond to the horny volar pads found on the feet of quadrupeds (see Fig. 549). Besides the elevations on the terminal phalanges there are five situated on the palm and sole at the base of the digits. Three others are situated on the proximal part of the palm. In the human foot the elevation corresponding to the hypothenar elevation of the palm undergoes a remarkable enlargement to cover the heel (Fig. 569, *f*).

Lines of the Palm [6].—The lines which cross the palm and the flexor aspect of the fingers are at the sites where the skin is folded when the hand is closed and used for grasping. Yet they are developed before movements occur in the foetal hand. When pads are being formed and papillary ridges developed, the cutis and epidermis, along the sites of

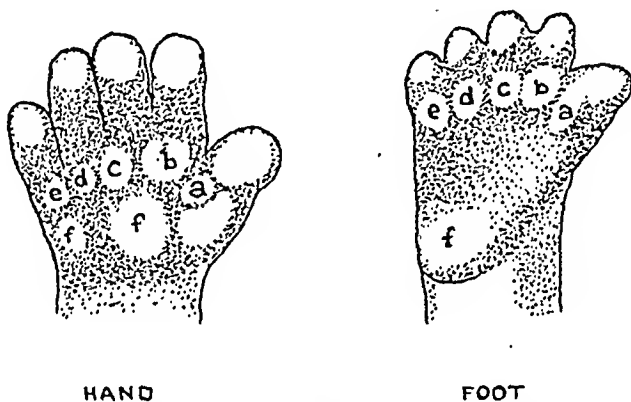


FIG. 569. The "Pad" Elevations on the Palm and Sole of a Human Foetus at the end of the 2nd month of development. (After Retzius.)
a, thenar pad; *b*, *c*, *d*, interdigital pads; *e*, minimal pad; *f*, *f*, proximal pads on palm and heel. Compare with Fig. 549, *A*, *B*, *C*.

flexion lines, remain undeveloped and bound to the underlying subcutaneous tissue. Fig. 570, taken from Dr. Würth's monograph, shows the order in which the lines appear in the foetal palm, *I*, appearing in the 8th week, *IV*, the last, during the 14th week. In the palm of the ape, *II* takes the position shown in Fig. 570 as *II'*; this transverse or simian disposition of the distal transverse line occurs frequently in the palms of Mongolian idiots. In them, too, the little finger has often only two creases instead of the usual three (Penrose).

Hair [7].—Hairs begin to develop in the 4th month; although in some regions, such as the eyebrows and lips, their formation begins a month earlier. Morphologically a hair may be regarded as a dermal papilla which has sunk into the subcutaneous tissue and become capped by a process of epidermis (Fig. 571). Hairs appear to have been primarily touch organs, and are modifications of the touch bodies found in the

the manner in which new hairs are produced resembles that of teeth, viz. from processes of the original bud. Hairs appear first on the head and then on other parts of the body. In the human body fat deposited in the subcutaneous tissue takes the place of hair as a heat conserver. Certain sexual hair-growths appear at puberty on the face, pubes and axilla. Morphologically, the axillae correspond to the inguino-pubic region, and it may be that this homology will help to explain why the axillae as well as the groin should be the sites of sexual hair, for there is a persistent tendency towards symmetry of development in the upper and lower extremities (see p. 598). The primitive mammary ridges, also sexual structures, end at the axilla and groin.

Hairs as they grow out from the skin are set at a definite angle, so that there is a characteristic pattern or slope for each field of the body. On the human body the hair slopes are apt to vary, but on the whole they are nearly the same as in the anthropoid body, the greatest difference

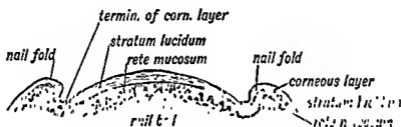


FIG. 573. Diagrammatic section across a Nail

lying in the frequency with which the hairs on the dorsal aspect of the human trunk are directed upwards (headwards) instead of downwards as in anthropoids [7].

Nails.—The nails are made up of three strata, representing the basal layer of cylindrical cells, the stratum mucosum and the stratum lucidum of the skin, the corneous layer being lost after the 4th month of foetal life. They appear first in the 3rd month as fields of thickened epidermis, on the tips of the digits (Fig. 554), but are afterwards shifted dorsally, carrying their palmar nerves with them, so that the terminal phalanx is wholly supplied from the palmar digital branches. At the end of the 3rd month the germinal layer of epithelium at the proximal margin of the nail field forms a lamina which grows into the dermis to form the root and is thus overhung by a reflection of skin—the *nail fold* (Fig. 574). The nail of the little toe, a digit in a retrograde phase of development, is frequently shaped like a claw, probably a reversion to a primitive form. The nail is produced on the scattered papillae (the matrix) at its root. The area of production is marked by the lunule. On the nail bed, in front of the lunule, the papillae are arranged in longitudinal rows.

shown in Fig. 572. As the follicle grows downwards the fundus of its shaft expands to form a bulb. Outside the follicular bulb mesodermal cells collect to become a papilla. Presently the bulb is invaginated by the papilla, which thus becomes clothed by the *central* cells of the basal stratum, while the surrounding wall of the bulb is lined by *peripheral* basal cells. On the papilla and within the *shaft* of the follicle is produced a mass of cells—the hair cone (Fig. 572, C)—the first rudiment of a hair. The central cells on the papilla give rise to those which form the core or pith of the hair shaft; they represent the stratum lucidum of the epidermis and the sheath of Henle in the hair follicle (Fig. 571, j). The cortex of the hair corresponds to the deep cells of the stratum corneum

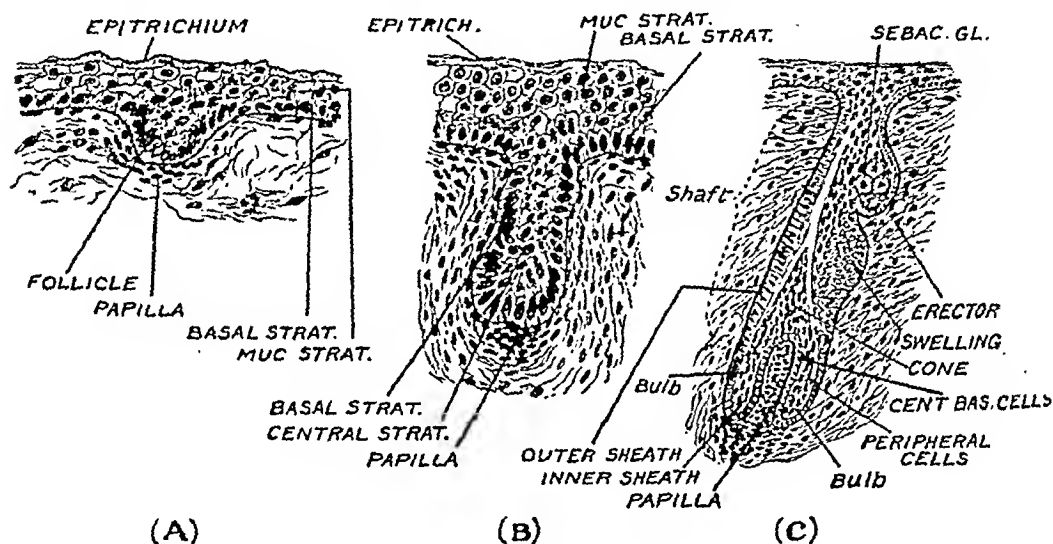


FIG. 572. Three Stages in the Development of a Hair Follicle. (After Stöhr.)

A. Hair follicle commencing to form in a foetus of 3 months.

B. The downgrowth of the follicle and mesodermal thickening to form papilla.

C. Invagination of follicular bulb by papilla with formation of matrix cone.

Erector, arrector pilae.

and to the sheath of Huxley of the hair root (Fig. 571, k). The outer root sheath is formed by the lining cells of the follicular shaft. As will be seen from Fig. 572, C, a sebaceous gland is produced from the shaft of the hair follicle, while the arrector muscle (Fig. 571, h) arises from the shaft at a deeper level. Like the muscles of the iris the arrector is peculiar in that it arises from cells of the ectoderm.

The hairs produced at the 4th month are fine in texture (*lanugo*), and by the 7th month the whole body is covered by them. The hair roots of the eyebrows, eyelids and of the lips and scalp are the first to appear. The production of hair-buds goes on until birth, the later buds and hairs being thicker and stronger. After birth, new hairs are constantly reproduced within the sheaths to replace the old (Fig. 571). Probably

the acini of the mammary gland, also believed to be highly modified sweat glands. The axillary glands contain much epithelial debris. They appear to be sexual in nature. The wax glands of the external auditory meatus are also modified sweat glands, being of the apocrine type. In man the apocrine type occurs in the situations just named (also in the circumanal region), whereas in other primates this type is more widely distributed.

Sebaceous Glands.—The sebaceous glands are outgrowths from the more superficial part of hair-huds (Figs. 571, 572). Their epithelial lining is derived from the germinal layer. In hair sheaths which have become occluded after their hairs have been shed or lost or when the mouth of a gland is blocked, the secretion is retained, and a sebaceous cyst or wen, so frequently seen in the scalp, is produced. Round the mouth, on the lips and nose the sebaceous glands, especially in hormonal disorders of the sexual system, are apt to retain their secretions and become inflamed, small pustules being thus produced. The Meibomian glands in the eyelids are modified sebaceous glands. At birth the child is covered by the vernix caseosa, which is composed of desquamated corneous epithelium and the secretion of sebaceous glands.

MAMMARY GLANDS

Evolutionary History [11].—It is a remarkable fact that although the milk glands do not come into use until adult life and although they must be regarded as among the later evolved structures of vertebrate animals, yet they are the first of all the glands arising from the epidermis to appear during development of the embryo. In the human embryo of the 6th week or in the corresponding stage of a pig (Fig. 575), or of any other mammal, the *primary mammary ridge* or milk line—a mere surface thickening of the ectoderm—is seen extending along the body wall on either side from axilla to groin. Bresslau regarded these primary ridges as representatives of the brooding organs of the ancestors of mammals, from which structures he supposed that the mammary glands were evolved [12]. In a large number of human beings (15%) one or more supernumerary nipples are to be found between the axilla and groin (Fig. 576), indicating the wide distribution of ancestral glands [13]. There is no longer any doubt that the mammary acini and ducts have been modified from sweat glands; a mamma represents a group of sweat glands developed from a circumscribed area of skin lying under the primitive mammary ridge [14]. Nor are there two opinions as to the stages in the evolution of the human nipple; they are repeated in its development. In its primitive form the nipple is represented by a

If the nail be pressed, as by the boot, the lateral papillae, under the nail fold (see Fig. 573) are directed downwards, and their epithelial outgrowths follow the same direction, thus causing ingrowing nail.

About the end of the 7th month the matrix of the nail root becomes differentiated, active growth sets in and the terminal margin of the nail becomes free; it grows forwards over the corneous layer which covers the terminal row of papillae of the nail bed. The ridge of corneous epithelium under the nail-tip represents the central part of the hoof ("frog") of ungulates (Fig. 574).

The nail is carried by the terminal phalanges. Prof. Leboucq observed that the tip of the terminal phalanges of the foetus is covered by a special fibrous cap (Fig. 574), which undergoes ossification directly from

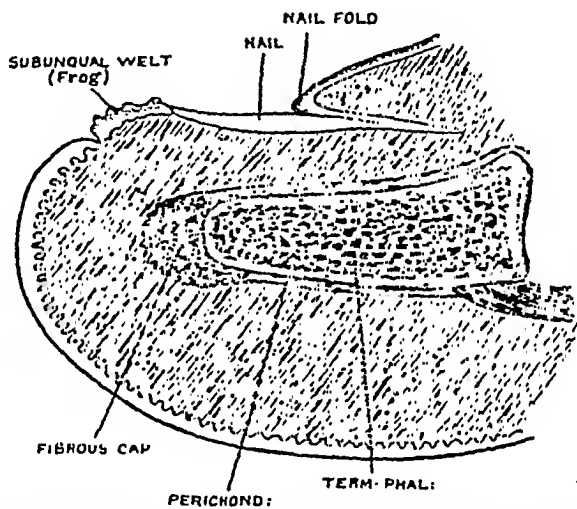


FIG. 574. Diagrammatic section of the Terminal Joint of the Digit of a Human Foetus to show the Cap of the Terminal Phalanx and the Subungual Welt.

membrane, while the rest of the phalanx is laid down and ossified in cartilage. The terminal phalanges have thus a special element added to them for the support of the nail and for the fixation of the terminal bulb of the digits.

Sweat Glands.—In the 4th month solid processes of epidermis grow into the dermis from the ectodermal troughs and also from the necks of hair follicles and produce sweat glands (Fig. 567, B). They arise at the same time and in the same manner as, and often in common with, the buds of hair roots and sebaceous glands [9]. They are produced within the epidermal ridges, and hence the ducts of sweat glands, as may be seen on the palms and fingers, open along the summits of these. The sweat glands in the axilla are peculiar [10]. Ordinary sweat glands are of the simple or *epicrine* type, whereas those of the axilla are of the compound or *apocrine* type. In section the axillary glands resemble

The *Female Breast* is composed of two embryological elements: (a) Glandular tissue derived from the ectoderm by a process of in-budding; (b) An intricate arrangement of connective tissue derived from the mesodermal subcutaneous tissue over the pectoralis major.

Seven stages may be recognized in the developmental history of the glandular mammary tissue. Four of these take place *before birth*:

- (i) The stage represented by the ectodermal ridge passing from axilla to groin—formed during the 6th week (Fig. 577, A).
- (ii) The production of a hump-like downgrowth of ectoderm from the

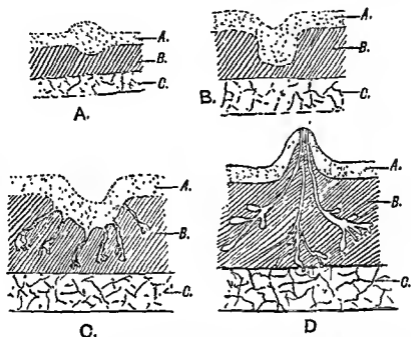


FIG. 577. Showing the various stages in the Development of the Mamma
 A, during the 2nd month; B, at the commencement of the 3rd month; C, at the 5th month; D, at birth.

A. = ectoderm; B. = subcutaneous tissue (mesoderm); C. = pectoralis major.

pectoral part of the mammary ridge. This downgrowth represents the pocket form of nipple (Fig. 577, B).

(iii) From the deepest stratum of the ectodermal bulh arises a number of solid bulbs, exactly similar to those of sweat glands (5th month). The stalks of these buds form the epithelial lining of the lactiferous ducts (Fig. 577, C).

(iv) The lobular buds, for each bud develops into a lobe, subdivide at their growing extremities. At first solid, they begin to canaliculize (7th to 9th months). At or about birth the pit or depression, from which the lobular buds originated, is raised, evaginated and forms the surface of the nipple (Fig. 577, D). Thus the ducts come to open on the apex

pocket—an invaginated area of mammary skin—on the wall of which milk ducts open. This pocket—an inverted nipple—becomes everted, chiefly by a proliferation of the tissues round the terminal parts of the duct, which raises the interior of the pocket first to the level of the surrounding skin and then above it to form a nipple—an everted mammary pocket. Further, the mammary ridge appears in both sexes alike, but this may not mean that both sexes of ancestral mammals were concerned in brooding or gave milk. The male is the father of girls as well as of boys; it is therefore necessary to provide both father and mother with a complete sexual outfit if each sex is to provide equal shares

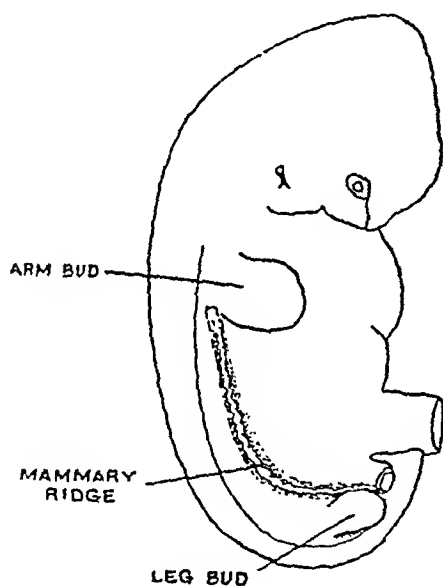


FIG. 575.

FIG. 575. Embryo of a Pig, showing the Mammary Ridge extending from Axilla to Groin. (After Schultze.)

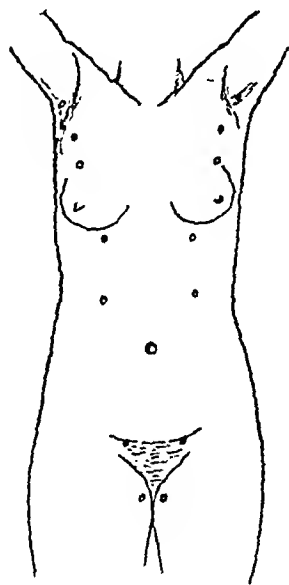


FIG. 576.

FIG. 576. Diagram to show the Position in which Supernumerary Nipples are usually found. (After Merkel.)

to the making of their progeny. In females the breasts undergo a great development at puberty, while in males they retain their infantile form. The mammary glands of a full-time foetus may enlarge under the influence of oestrone [15], which stimulates the maternal breasts, and hence after birth may yield a secretion (witch milk).

Oestrone acts chiefly on the duct system and interlobar tissues of the breast; the hormone supplied by the corpus luteum induces development of the secretory alveoli. Many endocrinologists attribute the growth and activity of the milk-forming tissue to prolactin, a hormone formed by the pituitary, particularly at the end of full term. Prolactin is also credited with a power of stimulating the maternal instincts [16].

Fat begins to be deposited in the subcutaneous tissue during the 5th month of foetal life. It forms a large element of the mammary gland after puberty. The subcutaneous tissue, out of which the capsule of the gland is formed, normally contains much fat. After lactation, when the glandular tissue atrophies to a considerable extent, a growth of fat replaces it. If no fat is deposited or if it be absorbed, then the breast loses its plump form and hangs on the chest.

Lymphatics.—We have already seen (p. 473) that during the 3rd month the skin and subcutaneous tissues become invaded by the developing system of lymph vessels, the pectoral system lying chiefly in the zone arising in connection with the jugular lymph sac. As each part of the capsule carries with it lymph vessels of the pectoral subdermal area [18] it will be seen that the arrangement of the parts of the capsule is an important matter in both the physiology and surgery of the gland. The *periductal* and *perilobular* lymphatics communicate through the *septal* or *interstitial* vessels with the *superficial mammary* and deep (*retromammary*) lymphatics (Fig. 578). The *superficial* communicate with the *subcutaneous*, the deep with those in the *pectoral sheath*: and thus it will be seen that mammary cancer may spread to the skin or pectoralis major. The deep and superficial join in the *circum-mammary* lymphatics, and from these pass *efferent vessels* to the *pectoral* and *central* glands of the axilla. The lymph passes from these to the deep axillary and inferior deep cervical glands—all of which are involved in late stages of cancer of the breast [19]. Other efferent vessels pass from the *circum-mammary* to the *anterior intercostal* glands of the upper four spaces; one or two vessels may go to the *cephalic* gland. During mammary hypertrophy, which takes place at the end of pregnancy, there is a further formation of lymphatic glands in the axilla (Stiles).

Peripheral Remnants.—Besides accessory ingrowths representing nipples, which are to be found in most foetuses of the 3rd month, isolated or semi-isolated small masses of glandular substance may be found situated in the *circum-mammary* tissue, beyond the body of the gland. Some may pierce the sheath of the pectoralis major, and become a source of recurrent cancer. The presence of glandular remnants is explained by the fact that when the primary budding takes place, the subdermal tissue is shallow and of small extent; in the subsequent growth of the thorax, the tissue in which the mamma is developed is widely spread out.

The mammary nerves (secretory) come from the 3rd, 4th and 5th intercostals; the nipple is supplied from the same nerves. The nipple

of the nipple. An ampulla is developed in each duct within the base of the nipple.

Stages after Birth.—Stage 5 occurs at puberty; the latent infantile lobular buds again undergo a rapid growth, and give rise to the minor lobules and acini. The breasts do not enlarge if the ovaries have been removed or destroyed by disease. Stage 6 occurs towards the end of pregnancy, and consists of a renewed production of glandular tissue. Stage 7 sets in with the menopause, and is characterized by an atrophy of the glandular tissue formed in the later stages of development.

In the process of sub-division, minor buds of adjacent lobes frequently

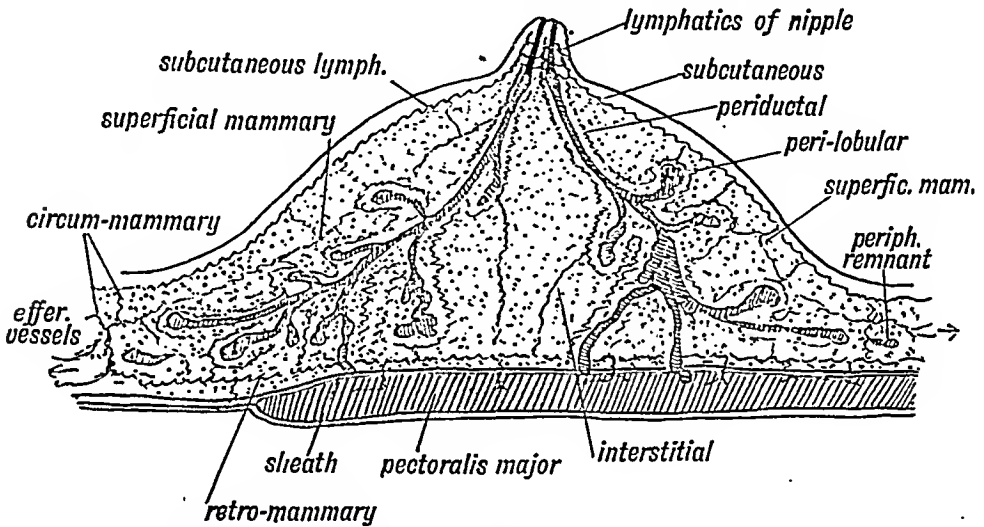


FIG. 578. Diagrammatic section of the Breast to show the Arrangement of its Capsule and Lymphatics. The lymphatic vessels are represented by thin wavy lines.

unite together. Hence it is found difficult, during dissection, to separate the gland into its primary lobes. In any of the three later stages a localized and invading hypertrophy of the cells of the glandular tissue may take place [17]. In this manner cancer begins. The part played by the lymphatics, which are situated in the mesodermal tissue of the gland, in the spread of this disease makes their study important.

Origin of the Capsular or Mesodermal Part of the Gland.—As the glandular buds grow into the subcutaneous mesodermal tissue, which reacts and hypertrophies around the invading processes, they divide it (see Fig. 578) into (a) superficial, and (b) deep layers, these being joined together by (c) interstitial septa. The superficial and deep layers are fused in (d), the circum-mammary tissue in which the final glandular buds terminate. The processes as they grew outwards also take on (e) perilobular and periductal sheaths. The deep and superficial layers are also connected with the anterior sheath of the pectoral muscles and the skin—for they are all parts of the same subdermal layer.

the dermal origin of neuroblasts is a factor of importance in the origin of the nervous system [23]. Although the various forms of touch bodies, such as the Pacinian corpuscles and those of Krause and Meissner, have not been traced developmentally, there can be little doubt that they arise directly from the epidermis beneath which they are situated [24]. Finer fibrils penetrate the epidermis; sensation in all its forms is localized at separate points [25].

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contains non-striated muscle, and is covered with touch papillae, and surrounded by modified sweat and sebaceous glands.

Dermis and Subcutaneous Tissue.—The subectodermal tissues, out of which the dermis and subcutaneous stratum are differentiated, is at first composed of cells of rounded outline embedded in a homogeneous jelly-like matrix. Mall regarded the matrix as a living substance in which, quite independently of the cells, connective tissue fibres are differentiated, both white and yellow. Processes are certainly developed from the cells, but it is doubtful if these ever become detached and form independent fibres [20]. At one time it was believed that part of each primary segment—named the *dermatome*—spread downwards into the somatopleure to form the dermis or true skin. Thus the dermis was regarded as segmental in origin. Dr. P. Murray excised part of the somatopleure of a chick before the corresponding paraxial segments had appeared, yet the part excised, when maintained alive, developed a normal dermis [21].

Fat Cells.—Certain granular cells of the connective tissue, especially of the subcutaneous layers, have the property of secreting *fat*, which appears first as diffuse droplets. These ultimately run together and produce the characteristic outline of adipose cells. Fat cells appear first in the subcutaneous tissue during the 5th month of foetal life; later it appears in the subserous tissue of the body wall. It reaches its greatest normal development just before and after birth. Two theories are held regarding the origin of fat cells: (i) that they are cells of the connective tissue differentiated and set aside permanently to form and store fat; (ii) they are ordinary connective tissue cells temporarily laden with fat [22]. There is present at birth a sharply differentiated mass of fat and lymphoid tissue in each posterior triangle of the neck and extending on each side beneath the trapezius muscle. Hatai regards this mass as the representative of the *interscapular gland* of hibernating mammals (see p. 474).

Touch Bodies and Sense Organs.—The cells of the ectoderm in the simpler forms of invertebrate animals not only protect the body but many of them become sensory or nervous in nature, developing processes which link them with neighbouring or even distant cells and thus are able to afford the animal data needed for a knowledge of its surroundings. In the development of the olfactory mucous membrane, of the auditory cells and of the taste buds of the human embryo, this specialization of areas of the ectoderm is seen (see Fig. 98). The retina, the brain, spinal cord and nerves are also areas of the ectoderm which have been highly specialized and set aside for the purpose of correlating the organism with its surroundings. Such cells may migrate and become grouped in central masses of the nervous system. Dart and Shellshear have shown that

INDEX

Aasar, Y. H., 61, 425, 426, 610
 Aaker, A. A. 161 171 176 202 204 319

Accessory processes of vertebrae, 99
 Achondroplasia, 641
 Achondroplastic skulls, 226
 Achromatin, 9
 Acoustic nuclei, 141
 Acrocephaly, 226
 Actomegaly, 166, 226, 239
 Actomion, 616
 Adair and Scammon, 232
 Adams, Julia L., 632
 Adams, W. E., 378, 474
 Addens, J. L., 153
 Adelmann, H. B., 153
 Adenoids, 369
 Adloff, P., 280
 Adrenal, Accessory, 561
 — cortex, Hormonal action of, 560
 —, Foetal cortex, 561
 Adrenals, Determining power of cortex,
 68
 — Development of 560
 Affenspalte, 190
 After-birth, 47
 Agdhar, E., 203
 Age changes in embryo and foetus, 76
 — estimation of, 76
 Air sacs, 484
 — sacs of Larynx, 493
 Akroyd and Zuckerman, 563
 Alar lamina, 122
 — process, 220
 Alimentary system, 379
 — tract, 25
 Alisphenoid, 220
 Allantois, 22, 543
 —, Origin of, 35, 36
 Allara, E., 378
 Allen, B. M., 509, 526
 Allen, C. M., 493
 Allen, E., 549
 Allis, E. Phelps, 231
 Altschule, M. D., 526
 Ameloblasts, 269
 — Evocation hy, 279
 Ammocoetes, Heart of, 423
 Amnion, 16, 19
 — Origin of, 34, 38

Amniotic adhesions, 71
 Amphibian respiratory system, 477
 Amphioxus, Gastrulation of, 57
 Amprino and Cattaneo, 649
 Amputations, Intrauterine, 71
 Amygdaloid body, 170
 Anal glands, 547
 — valves, 537
 Anders, H. E., 550
 Androgen, Action of, 509, 542, 543, 559
 Androsterone, 68
 Anencephaly, 72
 Angioblastic tissue, 20, 428
 Angiogenesis, 468
 Angular gyrus, 319
 Anlage, 19, 211, 589
 Anomalous muscles, 626
 Anseroff, N. J., 648
 Anson, B. J., 279, 342
 Anson and Black, 342
 Anson and McVay, 589
 Anson and Others, 320
 Anson and Wilson, 342
 Anthropoid, Implantation of Ovum, 16
 Anthropoids, Placentation of, 48
 Antrum of mastoid, 330
 Anus, Development of, 537
 —, Malformations of, 536
 Aorta, 356
 —, Arch of, 464
 —, dorsal, 359, 466
 Aortic arches, 356
 — arch, right, 358
 — sac, 356, 453
 Apocrine glands, 658
 Apostolakis, G., 648
 Appendix vermiformis, 416, 420
 Appleton, A. B., 499, 609, 644, 646, 648
 Aqueductus cochlea, 335
 Aqueous chamber, 306, 307
 Archenteron, 22, 57, 380
 Arch of foot, 624
 Arey and Others, 377
 Armadillo, Embryo productions in, 66
 Armstrong, P. B., 460, 526
 Arnold's nerve, 325
 Aron, Max, 47
 Arrector pilae, 656
 Arterio-venous anastomoses, 468
 Arteries, Anomalies of, 605
 Arteries, Formation of, 463
 Articular eminence, 259

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- Blood groups, 470
 — island, 428
 — supply of limb buds, 605
 — vessels, Formation of, 468
 Bloom, W., 404, 475
 Bloom and Bartlomez, 468, 475
 Blume, W., 103
 Body stalk, 23, 42
 — wall, Evolution of, 505
 Boeke, P., 130
 Boeker and Mueller, 631
 Boeker, H., 405
 Bohart, W. N., 104
 Bolk, L., 232, 280
 Bolk's law, 48, 655
 Bollinger, A., 563
 Bolton, J., 188, 203
 Bone, Architecture of, 646
 —, Formation of, 633, 636
 —, Induction of, 647
 — marrow, 471
 —, Nutrient vessels of, 641
 Bones, Growth of, 640
 —, Morphogenesis of, 640
 —, Ossification of, 638
 —, Remodelling of, 632
 Bonin, G. von, 203, 204
 Borghese, E., 647
 Botar, J., 116
 Botovansky, L., 590
 Botterell and Fulton, 154
 Boulgakow, S., 74, 010
 Bourne, G., 563, 564
 Bowdler, H. C., 280
 Bowel. See intestine.
 Boyd, Edith, 378
 Boyd, G. I., 204
 Boyd, J. D., 30, 74, 263, 355, 363, 474
 Boyden, E. A., 514, 527
 Brachet, A., 69, 233, 499
 Brachial artery, Anomalies of, 603
 — plexus, 601, 602
 Brachycephaly, 225, 608, 645
 Bradley, O. C., 320
 Brailsford, J. F., 648
 Brain, Development of arterial supply, 199
 —, Development of coverings, 201
 —, Expansion of, 209
 —, Principal fissures, 190
 —, Secondary sulci, 199
 —, Significance of arterial distribution, 200.
 —. See also under Central nervous system.
 Braine and Funck-Bretano, 378
 Brambell, F. W. R., 75, 526
 Brambell and Davis, 550
 Branchiae, 476
 Branchial, Use of term, 362
 — arch, Constituents of, 347
 — arches, 24, 343
 Branchial Arches, Changes in, 78
 —, Morphology of, 229, 231
 —, Nerve supply, 135
 Branchiomeres, 149, 347
 Brander, F. J., 172
 Brandes, G., 85
 Brandt, W., 294, 631, 665
 Brash, J. C., 232, 259, 264, 280, 281, 642, 647
 Brash and Stewart, 405
 Braus, A., 610
 Bregma, 214
 Bremer, J. L., 404, 485, 493
 Bresslau, E., 659, 666
 Brewer, J. L., 30, 48
 Brickel, A. C., J., 450
 Briscoe, Sir C., 590
 Broadbent, H., 280
 Brodie, A. G., 232
 Brodie and Others, 280
 Brock, van der 563
 Broman, I., 74, 115, 263, 264, 342, 404, 498, 666
 Bronchi, 483
 Bronchi, Growth of, 486
 Bronchus, Eparterial, 488
 Brooke, R., 630
 Broom, R., 232, 264, 630
 Broster, L. R., 563
 Broster and Vines, 75
 Browne, Dennis, 631
 Brouwer, B., 321
 Bruce and Walmsley, 631
 Bruenner's glands, 412
 Bruno, G., 631
 Bucher, O., 424
 Bulbar cushions, 450
 Bulbus cordis, 444, 453
 Bulla ethmoidalis, 289
 Bulloch, W., 559, 563
 Burkitt, A. N., 172
 Burkitt and Lightoller, 204, 363
 Burlet, H. M., 342
 Burne, R. H., 475
 Burns, R. K., 75, 523, 526, 627, 563
 Burr and Harvey, 204
 Burrows, H., 550, 563
 Bursa omentalis, 404
 Bursa pharyngea, 369
 Bystrow, A. P., 104
 Caeco-colic sphincter, 416
 Caecum, 416
 —, Development of, 417
 —, Developmental movements, 420
 Cairney, J., 363, 498
 Cairns, H. W. B., 527
 Calcar avis, 318
 Calcarine fissure, 196, 317
 Callender, G. W., 264
 Calloso-marginal fissure, 196

- Arteries, Lateral striate, 179
 — of limbs, 607
 Arytenoid cartilages, 491
 Asdell and Salisbury, 562
 Asdell, S. A., 85
 Ashley Montagu, M. F., 74, 549
 Ask, F., 320
 Ask-Upmark, E., 74
 Asterion, 214
 Astragalus, Changes in form, 622
 Astrocytes, 122
 Asymmetry, 483
 Ativism, 489
 Atlas, Articulations of, 98
 —, Morphology of, 93, 98
 Attraction sphere, 10
 Atwell, W. J., 155, 172, 404, 459
 Auditory meatus, External, 324
 — —, Internal, 340
 — movements, 337
 — nerve centres, 339
 — ossicles, 208, 329
 Audito-sensory areas, 340
 Auerbach's plexus, 112, 412
 Augier, M., 232
 Auricles, Formation of, 450
 Auriculo-ventricular valves, 458
 Autonomic nerves, Division of, 116
 — System, 116
 Axilla, Sweat glands of, 658
 Axis cylinder, 127
 —, Ossification of, 97
 Axons, Development of, 129
 Azygos lobe (abnormal), 498
 — — of lung, 488, 499
 Azygos veins, 434
- Badenoch, A. W., 563, 557
 Bagg and Little, 73, 75
 Bagg, H. J., 73, 75, 608, 609
 Baker, J. R., 563
 Ballatine, F. M., 498
 Ballatine, J. W., 74
 Barelay and Others, 474
 Barelay, M., 631
 Barcroft, Sir J., 48, 84, 131, 463, 474
 Bardeen and Lewis, 586
 Bardeen, C. R., 104, 425, 590, 609
 Barge and van Oijen, 499
 Barge, J. A. J., 75, 263, 045, 610
 Barlow, R. N., 590
 Barnard, J. W., 155
 Barnicot, N. A., 648
 Baron, M. A., 425
 Barrett, J. H., 648
 Bartelmez, G. W., 49, 342
 Bartholin's glands, 548
 Bartelmez and Evans, 155
 Basal and alar laminae, 134
 Bascom, K. F., 562
 Basilar membrane, 337
 Basilar plate, 216
 Basir, M. A., 405
 Bast, T. H., 342
 Basu, S. K., 648
 Baudrimot and Lachaud, 499
 Baxter and Boyd, 155
 Baxter, J. S., 30, 74, 527
 Bayer, F., 631
 Bayley, N., 323
 Beadle, O. A., 104
 Beams and King, 279
 Beansley, R., 378
 Beattie, J., 171, 417, 425
 Bell, Julia, 74, 610
 Bellairs, A., 294
 Bennett, H. S., 460
 Bensley, R., 498
 Bentley, F. H., 665
 Berg, R. C., 549
 Bergel and Gut, 405
 Bernstein, S. A., 232
 Berry, R. J. A., 203
 Berry Hart, D., 527
 Bevelander, G., 280
 Biceps cruris, 628
 — cubiti, 627
 Bile Ducts, 387
 Binocular angle, 309
 — vision, 295
 Biondi, D., 264
 Birds, Lungs, of, 485
 Birth, changes in circulation, 462
 — — in liver, 393
 — — in lungs, 490
 Bisgard, J. D., 647
 Bizarro, A. H., 631
 Blair and Davies, 155, 460, 474, 499
 Blair, Baesich and Davies, 115
 Blair, D. M., 499
 Blackfan, K. B., 85
 Bladder, Development of, 543
 — — of ventral wall, 535
 —, Muscles of, 545
 —, Origin of, 35
 —, Trigone of, 544
 Bland-Sutton, Sir J., 99, 222
 Blastema, 589, 595
 — of skeleton, 80
 Blastocyst, 14, 17
 Blastoderm, Artificial culture of, 68
 Blastopore, 52
 —, Dorsal lip of, 22, 63
 —, Interpretation of, 57
 Blastula, 13
 Blechschmidt, E., 320
 Bleicher and Beau, 103
 Blood circulation established, 26
 — corpuscles, Formation of, 468
 — corpuscles, Lineage of, 469
 — formation in chorion, 40
 — — in spleen, 397
 —, Formation of, 468

- Blood groups, 470
 — island, 428
 — supply of limb buds, 605
 — vessels, Formation of, 468
 Bloom, W., 404, 475
 Bloom and Bartlmez, 458, 475
 Blume, W., 103
 Body stalk, 23, 42
 — wall, Evolution of, 565
 Boeke, P., 130
 Boeker and Mueller, 631
 Boeker, H., 405
 Bohart, W. N., 104
 Bolk, L., 232, 280
 Bolk's law, 48, 655
 Bollinger, A., 563
 Bolton, J., 188, 203
 Bone, Architecture of, 646
 —, Formation of, 633, 636
 —, Induction of, 647
 — marrow, 471
 —, Nutrient vessels of, 641
 Bones, Growth of, 640
 —, Morphogenesis of, 646
 —, Ossification of, 638
 —, Remodelling of, 632
 Bonin, G. von, 203, 204
 Borghese, E., 647
 Botar, J., 116
 Botovansky, L., 590
 Botterell and Fulton, 154
 Boulgakow, S., 74, 610
 Bourne, G., 563, 564
 Bowdler, H. C., 280
 Bowel. See intestine.
 Boyd, Edith, 378
 Boyd, G. I., 204
 Boyd, J. D., 30, 74, 263, 355, 363, 474
 Boyden, E. A., 514, 527
 Brachet, A., 69, 233, 499
 Brachial artery, Anomalies of, 603
 — plexus, 601, 602
 Brachycephaly, 225, 508, 645
 Bradley, O. C., 320
 Brailsford, J. F., 648
 Brain, Development of arterial supply, 199
 —, Development of coverings, 201
 —, Expansion of, 209
 —, Principal fissures, 190
 —, Secondary sulci, 199
 —, Significance of arterial distribution, 200.
 —. See also under Central nervous system.
 Braine and Funck-Bretano, 378
 Brambell, F. W. R., 75, 526
 Brambell and Davis, 550
 Branchiae, 476
 Branchial, Use of term, 362
 — arch, Constituents of, 347
 — arches, 24, 343
 Branchial Arches, Changes in, 78
 — —, Morphology of, 229, 231
 — —, Nerve supply, 135
 Branchiomeres, 149, 347
 Brander, F. J., 172
 Brandes, G., 85
 Brandt, W., 294, 631, 665
 Brash, J. C., 232, 259, 264, 280, 281, 642, 647
 Brash and Stewart, 405
 Braus, A., 610
 Bregma, 214
 Bremer, J. L., 404, 485, 493
 Bresslau, E., 659, 666
 Brewer, J. I., 30, 48
 Brickel, A. C., J., 450
 Briscoe, Sir C., 590
 Broadbent, H., 230
 Brodie, A. G., 232
 Brodie and Others, 280
 Broek, van der 563
 Broman, I., 74, 115, 263, 264, 342, 404, 498, 666
 Bronchi, 483
 Bronchi, Growth of, 486
 Bronchus, Eparterial, 488
 Brooke, R., 630
 Broom, R., 232, 264, 630
 Broster, L. R., 563
 Broster and Vines, 75
 Browne, Dennis, 631
 Brouwer, B., 321
 Bruce and Walsley, 631
 Bruenner's glands, 412
 Bruno, G., 631
 Bucher, O., 424
 Bulbar cushions, 456
 Bulbus cordis, 444, 453
 Bulla ethmoidalis, 289
 Bulloch, W., 559, 563
 Burkatt, A. N., 172
 Burkatt and Lightoller, 264, 363
 Burlet, H. M., 342
 Burne, R. H., 475
 Burns, R. K., 75, 523, 526, 527, 563
 Burr and Harvey, 204
 Burrows, H., 550, 563
 Bursa omentalis, 404
 Bursa pharyngea, 369
 Byatrow, A. P., 104
 Caeco-colic sphincter, 416
 Caecum, 416
 —, Development of, 417
 —, Developmental movements, 420
 Cairney, J., 363, 498
 Cairns, H. W. B., 527
 Calcar avis, 318
 Calcarine fissure, 196, 317
 Callender, G. W., 264
 Calloso-marginal fissure, 196

- Cameron, J., 233, 320
 Cameron and Milligan, 342
 Campbell, D. K., 280
 Campbell, J. M., 499
 Campenhout, E., van, 342, 363
 Campion and Keith, 264
 Canalis reuniens, 334
 Capener, N., 104
 Capsular ligaments, 634
 Cardinal veins, 430
 Carey, Eben J., 418, 460, 589, 591, 647
 Carleton, Alice, 377, 527, 646
 Carmichael and Woollard, 321
 Carnegie Institution, 15
 Carotid body, 355
 — sheath, 466
 Carpenter, R. L., 609
 Carpus, Anomalous ossifications of, 621
 Carpus and tarsus compared, 618
 Cartilage bone, 211
 Cartilage, production from neural crest, 71
 Cattell, Psyche, 280
 Cave, A. J. E., 104, 172, 232, 426, 576, 590, 609, 621, 631, 648
 Cave and Haines, 264
 Cavernous sinus, 200
 Centra, 93
 Central fissure, 197
 — Nervous system, 117
 Centrosome, 10
 Cephalic index, 224
 Cerebellum, Centres and tracts, 141
 —, Functional nature of, 146
 —, Lobulation of, 142
 —, Origin of, 140
 —, Summary of origin, 145
 —, Vestibular connections, 340
 Cerebral cortex, Areas of, 188
 — —, Development of, 181
 — —, Differentiation of, 188
 — —, Localization of function in, 183
 — —, Projection of fibres to, 183
 — —, Supragranular, 198
 — vesicles, Expansion of, 174
 — vesicles, Origin of, 173
 Cerebro-spinal fluid, Control mechanism, 169
 — —, First formation of, 139
 — — system, 201
 Cerebrum, Origin of, 156
 —, Primitive divisions of, 184
 Cervical fascia, 576
 — malformations, 611
 — ribs, 90
 — sinus, 78, 347
 — spinous processes, 101
 — vesicle, 347
 Charles, C. M., 647
 Charles, S. W., 265
 Chavasse, B., 320
 Cheate, Arthur, 336
 Cheate and Cutler, 666
 Chemiotaxis, 27
 Chievitz, Organ of, 378
 Child, C. M., 65
 Childhood, Growth in, 83
 Chimpanzee, Growth of, 82
 Chin, Development of, 259
 Chlopin, N. G., 665
 Choana, 236, 249, 250
 Choanae, Atresia of, 251
 —, primitive, 286
 Choanoid muscle, 309
 Chondrification, Centres of, 633
 Chondrocranium, 205, 211
 Chorda tympani, 152, 352
 Chorio-allantoic grafts, 69
 Chorion, 15, 18
 —, Origin of, 34, 38
 Chorionic vesicle, 20
 — villi, 40
 Choroidal fissure, 177
 Choroid plexus, 177
 — tunic, 306
 Chromaffin cells, 562
 Chromatin, 9
 Chromosomes, 9
 —, x-y, 27
 Ciliary ganglion, 152
 — muscle, 308
 — processes, 301
 Cingulum, 275
 Circulation, Changes at birth, 462
 —, Early establishment of, 40
 —, Remnants of foetal, 464
 Circulatory system, 427
 Circumvallate papillae, 367
 Clarke, E. and E., 468, 473, 475, 590
 Clarke, W. E. Le Gros, 29, 154, 169, 171, 203, 321, 342, 589
 Clark and Blomfield, 590
 Clark and Russell, 171
 Clavel and Colson, 426
 Clavicle, 596, 616
 Clayton-Jones, E., 74
 Cleave, C. D., van, 459
 Cleft membrane, 346
 Cleido-cranial dysostosis, 616
 Clements, L. P., 498
 Clitoris, 538, 541
 Cloaca, 503
 —, Development of, 530
 —, Ectodermal, 533
 —, Metamorphosis of, 530, 532
 Cloacal folds, 538, 540
 — membrane, 52, 531
 Club foot, 622
 Cobb, W. M., 590
 Coccygeal body, 562
 — part of spinal cord, 120
 — vertebrae, 101
 Coccygeus, 628
 Coccyx, 89, 569

- Cochlea*, Evolution of, 322
 — ganglion of, 323, 337
 — nuclei, 339
Cockayne, E. A., 610, 665
Coeliac axis, 467
Coelom, Early development, 18
 —, Division of, 381
 —, Origin of, 58
 —, Parts of, 25
Coghill, G. E., 84, 131
Cohen and Davies, 154
Cohen and Friedman, 617
Cole, F. J., 475
Collateral fissure, 197
Colliculi, 315
Collins, D. C., 426
Coloboma, 303
Colon, Development of, 413
 —, Fixation of, 414
Colour vision, 310
Columella, 324
Colwell, H. A., 610
Colyer, Sir J. F., 280
Combs, J. D., 49
Commissure, Anterior, 186
Commissures of Brain, Development of, 185
Competencies of body segments, 102, 103
Conel, J Le Roy, 203
Congdon, E. D., 363, 341, 499
Conjoined tendon, 568
Conjugal ligament, 99
Conn and others, 499
Connective tissue, Theories of formation, 575
Connolly, C. J., 204
Constrictor urethrae, 576
Contat, C., 499
Contraheutes, 628
Convolutions, Formation of, 188
 —, Significance of, 190
Conway, E. A., 475
Cooper, Eugenia, 172, 563
Cooperman, M. B., 610
Cope, V. Z., 232
Coraco-humeral ligament, 627
Coracoid, 615
Cordebar, J., 631
Cornea, Development of, 298
Corner, G. W., 28, 30, 48, 405
Coronary circulation, 457
Corpora quadrigemina, 315
Corpus callosum, 187
 — — absence of, 188
 — luteum, 6
 — spongiosum, 542
 — striatum, 157, 170, 173, 177
 — striatum, Evolution of, 178
Corti, Organ of, 337
Costal processes, 99
Coventry and Others, 104
Cowdry, E. V., 29
Cowper's glands, 548
Crania, Abnormal, 226
Cranial axis, Flexion of, 227, 228
 — bones, Age changes in, 215
 — —, Growth of, 210
 — cavity, Growth of, 209
 — nerves, 314
 — —, Centres of origin, 155
 — —, Fifth, 279
 — —, Ganglia of, 354
 — —, Morphology of, 153
 — —, Nuclei of, 135
 — —, Segmental, 151
Cranio-pharyngeal canal, 165
Craniopagus, 65
Cranium, Evolution of, 205
 —, Membranous part, 210
Crawford, G. N. C., 617
Crew, F. A. E., 557, 563
Crew and Mirskaia, 665
Cribiform plate, 247
Cricoid cartilage, 491
Crisari, C., 378
Crucial ligaments, 635
Crusta petrosa, 271
Crymble, P. T., 405, 424
Cusajunco, F., 115, 590
Cultural methods, 69
Cummins, H., 631, 665
Cummins and Spragg, 665
Cunningham, D. J., 103, 193, 590
Cunningham and Telford, 232
Curli and Tromly, 563
Cushing, Harvey, 172
Cuticular membrane, 270
Cutis, Development of, 652
Cuvier, Duct of, 430
Cyclops, 70, 292
Cyclopia, 240
Cynodont teeth, 276
Cytoecesis, 154
Czarshi, C., 549

Da Costa, A. C., 564
Dalcq, A., 62
Dambrin, L., 527
Danchakoff, Vera, 320, 563
Dankmeyer, J., 610
Dantschakoff, W., 75
Dardinski, V. J., 405
Darlington, C. D., 29
Daron, C. H., 49
Dart, Raymond, 154, 172, 202
Dart and Shellshear, 664, 666
Darwin's tubercle, 326
Davenport, C. B., 83, 85, 631
Davies, D. V., 647
Davies, F. J., 30, 115, 460, 474, 631
Davies and Francis, 474
Davies, Gladstone and Stibbe, 115
Davies and Others, 590

- Davies and MacConaill, 460
 Davis, C. L., 459
 Deansley, Ruth, 550
 De Beer, G. R., 62, 73, 231, 233, 362
 De and Sinha, 527
 De Garis, C. F., 363, 459
 De Lange, D., 62, 154
 De Renyi, G. S., 280
 De Winiwarter, H., 29, 379
 Decidua, 31
 Decidua scrotina, 44
 Dees-Mattingly, H., 49
 Deibert, G. A., 549
 Delmas, J., 116
 Dendrites, 127
 Dendy and Nicholls, 148
 Dental alveoli, 272
 — follicle, 271
 — furrow, 267
 — lamina, 267
 — —, Separation of, 279
 — papilla, 269
 — sac, 271
 — shelf, 268
 Dentigerous cysts, 274
 Dentine, Origin of, 270
 Dentition, Milk, 266, 273
 —, Permanent, 273
 Dermal bones, 211
 — nerves, 665
 — papillae, 652
 Dermatomes, 664
 Dermis, 664
 Derry, D. E., 244
 Desai, P., 231
 Determination of parts, 593
 Detwiler, S. R., 116, 131, 609
 Detwiler and Laurens, 320
 Development, Acceleration of, 48
 —, Rates of, 82
 Diaphragm, 493
 —, Evolution of, 477, 566
 Diaphragmatic hernia, 493
 Diaphysial aclasis, 642
 — discs, 640
 Dichotomy of parts, 70
 Dick, J. Lawson, 280
 Dickie, Milne, 293
 Diem, F., 665
 Diencephalon, See thalamencephalon
 Dieulauf, R., 104
 Digby, K., 640, 647
 Digestion, Organs of, 379
 Digits, Abnormalities of, 608, 645
 —, Muscles of, 628
 —, Supernumerary, 620
 Dijkstra, O. H., 648
 Diploe of cranial bones, 214
 Dixon, A. F., 649
 Dodds, C. S., 647
 Dolichocephaly, 225
 Dominance of side, 70
 Doran, A., 549
 Doran and Keith, 526
 Dorso-cervical junction, 90
 Dorso-lumbar junction, 90
 Dorsum sellae, 220, 222
 Dott, N. M., 171, 426
 Dow, D. R., 104, 154
 Downman, C. B. B., 362
 Drennan, G. R., 203
 Drennan, M. R., 599, 609
 Drew, A. H., 74
 Drinker and Yoffey, 475
 Drinkwater, H., 610
 Drosophila, Chromosomes of, 11
 Duckworth, W. L. H., 499
 Ductless glands, Origin of, 401
 Ductus arteriosus, 357
 — caroticus, 358
 —, —, closure of, 463
 — endolymphaticus, 333
 — venosus, 438
 Duodenal diverticula, 413
 — loop, 401
 Duodeno-jejunal flexure, 409
 Duodenol-jejunal fossa, 423
 Duodenum, 406
 —, Fixation of, 406
 —, Malformations of, 413
 Dupas and Badelon, 631
 Duplication of parts, 70
 Dura mater, Origin of, 213
 Durward, A., 202
 Dustin, P., 405
 Duthie, E. S., 475
 Duthie, G. M., 526
 Dwight, T., 631, 632
 Dye and Kinder, 233
 Dysplasia foetalis, 72, 105

 Ear. See also under hearing
 —, Bones of, 208
 —, Development summarized, 341
 —, Evolution of, 322
 —, External, 325
 Economo, C. von, 203
 Ectopia vesicae, 544
 Eden, T., Watts, 95
 Edgeworth, F. H., 264, 320, 362, 499
 Edinger, Tilly, 232
 Edwards, H., 425
 Eighth cranial nerve, 338
 — —, Ganglion of, 323
 Eisenstaedt, J. S., 563
 Elder and Yerkes, 85
 Elftman, H. O., 589
 Elftman and Manter, 631
 Elliot-Smith, Sir G., 154, 178, 203, 320,
 589, 651
 Elliott, H. C., 647
 Embryo, Early stages in development, 13
 et seq.

- Embryo, Estimation of age, 76
 —, Formation of, 13
 — from 3rd to 5th week, 23
 —, Nourishment of, 34, 41
 — to foetus, 79
 Embryological healing, 240
 Embryonic plate, 21
 —, Mapping of, 58
 —, Sections of, 54
 Emmart, E. W., 378
 Enamel buds, 269
 — germs, Culture of, 279
 — organ, Remnants of, 272
 —, Origin of, 269
 Endocardial cushions, 452
 Endometrium, Recuperative power of, 49
 Epaxial muscles, 108
 Ependymal zone, 121
 Epiblast, See under Ectoderm
 Epibranchial placodes, 151, 347, 354
 Epicanthic fold, 312
 Epicritic theory, 114
 Epididymis, 551
 Epiglottis, 367, 491
 —, Position of, 492
 Epignath, 64
 Epinasse, P. G., 172
 Epiphysal lines. See Diaphysal
 Epiphyses, Aberrant, 640
 —, Formation of, 640
 —, Nature of, 643
 Epiphysis. See pineal body
 Epi-sternum, 582
 Epithalamus, 159
 Epitrichium, 650, 651
 Epitrochleo-anconeus, 627
 Epophoron, 507
 Erect posture, 566
 —, Adaptation to, 486, 488
 Ernyi, I., 320
 Eruption of teeth, 277
 Erythroblasts, 468
 Erythrocytes, 468, 470
 Eternod, A. C. F., 92
 Ethmoid, 242, 247
 —, Development of, 222
 —, Growth of, 288
 Ethmoidal cells, 289
 Eustachian tube, 324, 327, 349
 — valve, 448
 Evans and Krah, 609
 Evans, Arthur, 425
 Evans, H. M., 75, 341
 Evans, L. T., 405
 Evatt, E. J., 550
 Evocation by lymphoid tissue, 374
 — of drum-membrane, 331
 — — otocyst, 335
 Eyc. See also under sight.
 —, Development of, 295
 —, Nature of, 295
 —, Tunics of, 306
 Eyeball compared with brain, 319
 —, Development of, 296
 —, Growth of, 310
 Eyelashes, 312
 Eyelids, Development of, 311
 Eye tunics compared to brain membranes, 308
 Face changes at puberty, 289
 —, Development of, 78, 235
 —, Evolution of, 234
 —, Malformations of, 70, 238
 —, Muscles of, 350
 Facial angle, 227
 — nerve, 152
 Fahmy, N., 155
 Fairbank, H. A. T., 630
 Falciform ligament, 390
 Fallopian tube, 7
 Fang-Dechau, 631
 Fasciae, 572
 Fat, Formation of, 663, 664
 Fawcett, E., 219, 263, 631
 Fell and Canti, 640
 Fell and Gruenberg, 647
 Fell and Landauer, 647
 Fell and Robison, 647, 648
 Fell, Honor R., 69, 270, 342, 609, 643
 Femoral canal, 569
 Fenestra ovalis, 353
 Fertilization of ovum, 13
 Fibre cells, Formation of, 575
 Fibre formation in connective tissue, 664
 Fieandt and Saxem, 342
 Fifth cranial nerve, 314
 Filum terminale, 120
 Finley, E. B., 264, 475
 Fischer, E., 233
 Fischer, H., 104
 Fish, Respiratory system of, 476
 Fisher and Ransom, 115
 Fistulae of ear, 326
 — of pinna, 341
 Fissure of Rolando, 197
 — of Sylvius, 191
 Fissures, first temporal, 319
 — of brain, 190
 — — Classification of, 191
 — Inferior frontal, 198
 Fitzgerald, R. R., 631
 Fitzwilliams, D., 631
 Flecker, H., 631, 648
 Fleming, A., 626
 Fleming, R. M., 85
 Flexner and Stiehler, 154
 Flexor accessorius, 624

- Flexures or bends of neural tube, 148
 Floccular fossa, 336
 — lobe of cerebellum, 142
 Florian, J., 30, 544
 Flynn, T. T., 29
 Foetal dysplasia, 72
 — membranes, Evolution of, 34
 Foetus, at full-time, 80, 81
 — Estimation of age, 77
 —, Tables of growth, 83
 Foley, L. D., 342
 Folley and Others, 666
 Follicular cells, 5
 Fontanelles, 214
 Foot. See also Tarsus
 —, Development of arch, 622
 —, Eversion of, 622
 —, Modifications for walking, 622
 —, Morphology of, 617
 Foramen magnum, Formation of, 216
 — ovale, 223, 453, 463
 — of Majendie, 139, 202
 — — Monro, 174
 — primum, 453
 Foramina in bone, Formations of, 222
 Forbes, G., 666
 Forbes, T. R., 28
 Fore-brain, 119, 156
 —, Development of, 157
 —, Flexure of, 148
 —, Introduction to study of, 169
 —, Map of areas, 169
 —, Sensory pathways of, 160
 Fore-gut, 22
 Forehead, Evolution of, 222
 Forster, A., 631
 Fourchette, 539, 541
 Fovea centralis, 302
 Fraude, F., 362
 Fraedrich, G., 610
 Francillon, M. R., 460
 Frankfort plane, 225
 Franklin and Others, 474
 Franklin, K. F., 459
 Franz, V., 264
 Frasin, I., 362
 Frazer and Whitehead, 115
 Frazer, J. E. S., 84, 154, 263, 267, 341, 347, 362, 424, 498, 549
 Free martin, 67, 559
 Freud, J., 29
 Frey, Hugo, 342
 Friedel, H., 666
 Friedenthal, F., 655, 665
 Frontal bone, 211
 Frontal sinus, 288
 Fronto-nasal process, 233, 236
 Froriep, E., 562
 Froriep's ganglion, 153
 Fuchs, F., 526
 Fuerst, C., 320
 Fujita, T., 341
 Funicular process, 556
 Furcula, 367
 Futamura, R., 363
 Gadow, Hans, 95, 104
 Gall-Bladder, 387
 —, Absence of, 388
 Galls, Formation of, 65
 Ganglia, Cranial, 150
 — of cranial nerves, 153, 354
 — of posterior roots, 111
 —, sympathetic, 112
 —, vertebral, 111
 Gardner, W. U., 48, 563
 Garraud and Bartiez, 499
 Gartner, Duct of, 507
 Gaskell, J. F., 104
 Gaskell, W. H., 116, 118, 166, 172, 233
 Gaskell's Theory, 231
 Gastrocnemius, 621
 Gastro-hepatic omentum, 390
 Gastrulation, 57
 Gatzki, W., 460
 Gayet, R., 632
 Geddes, Auckland, 590, 598, 609
 Genes, 11
 Genetics. See under Chromosomes
 Geniculate body, lateral, 315
 Geniculate ganglion, 323, 337
 Genio-glossus, 366
 Genital cord, 505, 516
 — eminence, 538
 — folds, 549
 —, inner, 535, 538
 — organs, external, 538
 — —, — of female, 541
 — —, — of male, 542
 — ridge, 27, 504
 — septum or cord, 517
 Genna, G. E., 204
 Gennari, Line of, 317
 Genotype, 68
 George, W. C., 30
 Germinal epithelium, 5
 — vesicle, 9
 Germplasm, Experiments on, 73
 Gersh, I., 172, 526
 Gestation, Length of, 80
 Gibbs, E. and F., 204
 Gilbert, M. S., 171, 172
 Gill arches. See Branchial.
 Gillies, C. D., 620, 631
 Gilmore, J. R., 475
 Gilse, P. H. G., van, 232
 Gingival groove, 266
 Ginglinger, A., 425
 Giraldes, Organ of, 508
 Girgis, A., 563
 Gladstone and Cockayne, 499
 Gladstone and Dunlop, 154, 204
 Gladstone and Wakeley, 169, 172, 590

- Gladstone, R. J., 30, 104, 363, 378, 459
 Glasstone, S., 281
 Glees, P., 132, 203
 Glees and Clark, 171, 321
 Glck, B., 609
 Globular process, 236
 Glomerulus, 500
 Glosso-pharyngeal nerve, 153, 353
 Glottis, 490
 Gluckmann, A., 293, 590, 609, 647
 Goddard, T. R., 562
 Godwin, M. C., 378
 Goeppert, E., 665
 Goldby, F., 154, 171, 202, 203
 Goldner, J., 475
 Goldschmidt, R., 29, 74, 549, 563
 Goldsmith and Butter, 460
 Goldstein and Stanton, 280
 Goldstein, M. S., 265
 Golub, D. M., 363
 Gonadotrophic hormones, 7, 47
 Goodrich, E. S., 601, 609
 Goormaghtigh, N., 363, 527, 664
 Gordon-Taylor and Handley, 378
 Goss, C. M., 459
 Gowar, F. J. S., 627
 Graafian follicle, 6
 Gracila and Cuneate nuclei, Origin of, 136
 Graening, W., 649
 Grant, J. C. R., 425
 Granulocytes, 470
 Graves, W. W., 630
 Gray, J. H., 476, 665, 666
 Gray, P., 626
 Great toe. See Hallux.
 Greene and Laurens, 342
 Greene, R. R., 74
 Greene, H. L., 104
 Gregg, N. M., 74
 Gregory, W. K., 263, 280, 589, 609, 631
 Greig, D., 254, 264, 426
 Greil, A., 460
 Grenlich, W. W., 74, 630
 Grigoire, G., 378, 405
 Grosser, O., 30, 48, 372
 Groth, G., 425
 Growth, Comparative rates of, 82
 —, Dominance of centres, 70
 —, Growth, Tables of, 83
 Gruenberg, H., 649
 Grünwald, P., 74, 526, 562
 Grzybowski, J., 203
 Gubernaculum dentis, 273
 — testis, 518, 552, 554
 Guest, Edith, 666
 Gulland's theory of lymphoid tissue, 370
 Gut, Demarcation of, 380
 Gutmann, E., 590
 Gutmann and Young, 590
 Guttierrez, R. A., 425
- Habenula, Ganglion of, 167
 Haemoblasts, 469
 Haemolymph nodes, 474
 Haidenhain, M., 526
 Hain and Robertson, 527
 Haines, R. W., 115, 588, 589, 591, 632, 645, 646, 648
 Hair, G. W., 172
 Hair, Development of, 654
 —, Grouping of, 650
 Hairlessness, 651
 Hair slopes, 657
 Hakin, M., 630
 Haldane, J. B. S., 29
 Hallux, Muscles of, 624
 Halpert, B., 405, 425
 Ham, A. W., 647
 Hamilton, J. B., 563
 Hamilton, W. J., 28, 29, 61
 Hammar, J. A., 329, 570, 589
 Hammond and Others, 549
 Hammond, W. S., 363
 Hand. See also Carpus.
 —, Development of, 594
 —, Morphology of, 617
 Handley, W. Sampson, 666
 Hanson, F. B., 690, 631
 Hardy, Mary, 342
 Hare-lip, 238
 Harlant, M., 563
 Harpman and Woollard, 279, 281
 Harris and Thomson, 460
 Harris, C. B., 29
 Harris, H. A., 84, 85, 100, 104, 105, 215, 232, 280, 475, 549, 690, 631, 640, 641, 647
 Harris, Walfrid, 610
 Harrison, R. G., 69, 73, 129, 132, 689, 594, 609
 Hartman, G. G., 28, 29, 47, 48, 49, 85
 Harvey and Zimmerman, 499
 Hassall's corpuscles, 373
 Hastings Ince, J. G., 104
 Hauser, C., 404
 Haversian canals, 638
 Hayek, H. von, 499
 Head, Ghanges in, 79
 —, De Lange's theory of, 62
 —, Determination of shape, 225
 Head-process, 22, 54
 Head, Sir Henry, 114
 Hearing, Structures connected with, 322
 Heart, 427
 — as placental pump, 440
 —, Changes in position, 464
 —, Conducting system, 461
 —, Demarcation of chambers, 444
 —, Development of, 440
 —, Ectopia of, 466
 —, Fixation of, 429, 464
 —, Later stages in evolution, 428
 —, Malformations of, 455, 457

- Heart, Septa of, 452
 Heidenach, J. C. R., 154
 Heidsieck, G., 104
 Heinbach, W. F., 378
 Hellman, M., 262, 280, 377
 Henle, Loops of, 512
 Hensen's node, 22, 53
 Hepatic veins, 437
 Herberg, K. A., 405
 Herdorfer and Scammon, 203, 231
 Heredity. See under Chromosomes and Genes.
 — of injuries to germplasm, 73
 Hermaphrodites, 67
 Hernheiser and Kubat, 499
 Hernia, 567
 — diaphragmatic, 493
 Herrick, Judson, 169, 202, 203
 Hertig, A. T., 30, 48
 Hertwig's sheath, 272
 Heschl's gyri, 340
 Heslop, T. S., 171
 Heterochrony, 82
 Hett and Butterfield, 378
 Heuser, C. H., 16, 30, 459, 499, 526, 528
 Hewer, Evelyn, 85, 115, 591
 Hiatus semilunaris, 287
 Hibernating gland, 472
 Hill, J. P., 29, 40, 48, 522, 528
 Hill, Sir L., 577
 Hill, W. C. O., 131, 499, 563
 Hind-brain, 119
 —, Demarcation of, 133
 —, Vital centres of, 133
 Hind-gut, 22
 —, Parts derived from, 413
 Hines, M., 202, 321
 Hintzsch, E., 378
 Hip, Congenital dislocation of, 614
 Hip-joint, 596
 Hippocampal commissure, 186
 — formation, 285
 Hippocampus, 179
 Hirsch, E. W., 550
 Hirst, A., 116
 His, Prof. Wm., 263, 451
 Hochstetter, F., 153, 204
 Hodler, D., 563
 Hoedemaker, C., 49
 Hogben, L., 263
 Holland, C. T., 631
 Hollinshead, W. H., 363, 564
 Holyoke, E. A., 405
 Homma, H., 75
 Hooton, E. A., 589
 Hormones, Action on Skin, 651
 — Gonadotrophic, 7
 Horowitz, E., 426
 Hou-Jensen, H. M., 377
 Howell, A. B., 115, 631
 Hrdlicka, A., 265
 Huber, E., 265, 363
 Huber, G. C., 526
 Huffman, E. F., 527
 Huggins and Others, 281
 Hughes, F. F. W., 475
 Hummel, K. P., 475
 Humphrey, R. R., 75, 549
 Hunter, John, 65, 67, 563, 642, 648
 Hunter, R. H., 74, 104, 424, 425, 516, 520.
 527, 549, 563
 Huntington, G. S., 499
 Humerus, Torsion of, 598
 Humphrey, R. R., 563
 Hurrell, D. J., 645, 648, 649
 Huxley, Julian, 65, 69, 74
 Hyaloid artery, 306
 — canal, 307
 Hydatids of testis, 524
 Hydatid, stalked, 508
 Hydrocephaly, 216
 Hymen, 521, 526
 Hyoid arch, 327, 351
 — bone, 351
 Hyo-lingual, 352
 Hyo-mandibular cartilage, 253, 324
 Hypernephromata, 561
 Hypobranchial eminence, 480
 Hypochondral bow, 93
 hypocone, 280
 Hypoglossal nerve, 354
 Hypoischium, 613
 Hypospadias, 541
 Hypothalamus, 156, 159, 162
 Iagnov, 460
 Iasswain, G., 590
 Ichthyosis, 651
 Ileo-cacal fossae, 422
 — valves, 421
 Ileo-colic sphincter, 416
 — colon, 416
 Ilium, 612
 Incisor teeth, Position in biting, 281
 —, Blood supply of, 244
 Incus, 324, 329
 Induction by the duct of pronephros, 502
 Infra-cardiac bursa, 389
 Ingalls, N. W., 363, 442, 459, 502, 649
 Ingalls and Grossberg, 648
 Inglis, K., 476, 666 ✓✓
 Inguinal canal, 555, 567
 —, Formation of, 518
 — fold, 518, 558
 — ligament, 553
 — region, 567
 Inner cell mass, 14
 Innominate vein, 432
 Inter-articular cartilage, 259, 633
 — ligaments, 635
 Interchondral discs, 633
 Inter-clavicle, 616
 Inter-costal vein, Left, superior, 432

- Intercoastal muscles, 108, 587
 Intermediate cell-mass, 25, 59
 Inter-parietal, 223
 Interscapular body, 473, 664
 Intersegmental septa, 93
 Inter-Sex, 559
 Inter-sigmoid fossa, 415
 Interstitial cells, 553
 Interventricular foramen, 457
 Intestinal loop, 409
 — —, Abnormal rotation of, 424
 — —, Rotation of, 409
 Intestines, Differentiation of coats, 412
 — —, Diverticula of, 412
 — —, Malformations of, 412
 Intra-parietal fissure, 198
 Intrauterine amputations, 71
 Iris, Muscles of, 308
 Irving, A. and E., 280
 Ischiopagus, 65
 Ischium, 613
 Island of Reil, 175, 191
 — —, Opercula of, 193
 Israels, M. C. G., 475
 Iter venosum, 431, 478, 482
- Jablonsky and Meyer, 131
 Jackson, J. L., 475
 Jacobson's Organ, 241, 246, 253, 290
 Janghans, H., 104
 Jayle, G. E., 293
 Jefferson, G., 204
 Jeker, L., 495
 Jenkins, G. B., 231
 Jenkinson, J. W., 329, 342
 Job, Leibold and Fitzmaurice, 263
 Johnson, E. H., 264
 Johnson, F. P., 404, 425, 549, 562
 Johnston, T. B., 30, 154, 425, 610
 Joints, Development of, 633
 Jones, O. W., 131
 Jones, R. L., 362
 Jones, Tudor, 460
 Jordan, H. E., 77, 425, 473, 475, 563
 Jordan and Horsley, 378
 Jordan and Kindred, 665
 Josselyn, L. E., 498
 Juba, A., 131
 Judson, Herrick C., 172
 Jugular, lymph sac, 472
 — vein, Primitive, 200
 — veins, 433
 Junctional ring, 43
 Junctional tubules, 509
- Kaan, Helen W., 342
 Kallus, E., 364, 377, 499
 Kampmeier, O. F., 475, 512
 Kantor, J. L., 425
- Kantor, S., 75
 Kappers, Ariens, 136, 154, 203, 294
 Kardasewitch, B. I., 405
 Karlstroem, S., 280
 Karyokinesis, 9
 Kassatkin, S., 632
 Katznelson, Z. S., 115, 590
 Keen, J. A., 460, 474
 Keene, M. F. Lucas, 154
 Keene and Hewer, 131, 172, 378, 527, 561
 Keith, Sir A., A., 75, 104, 172, 203, 233, 263, 265, 280, 341, 362, 460, 498, 599, 631
 Keith and Flack, 460
 Keith and Tweedie, 172
 Kelly, D. Brown, 293
 Kennedy, W. P., 563
 Kennedy and Clark, 474
 Kerekring, Bone of, 218
 Kerr, Sir J. G., 60
 Kershman, J., 131
 Kesteren, H. L., 231, 232
 Key, W. C., 74
 Keyes and Edwards, 104
 Kidd, Walter, 665
 Kidney, Abnormalities of, 514
 — Blood supply of, 513
 —, Growth of, 512
 —, Movements of, 513
 —, Nerve supply of, 114
 —, Origin of, 510
 Kindred, J. E., 30, 475
 King, D. H., 647
 King, J. D., 280
 King, L. S., 203
 Kingsbury, B. F., 154, 378, 562
 Kingsbury and Roemer, 172
 Kingsbury and Rogers, 378
 Kirk, John, 405, 563
 Kirschbaum and Downey, 475
 Kiss, F., 115, 165
 Kisselbach, A., 563
 Klein, M., 47
 Knee-joint, 635
 Knobloch, D. von, 173
 Koff, A. K., 527
 Koffman, V., 564
 Koganei, Y., 281
 Koller, P. C., 29
 Kondratjew, N., 564
 Kosinski, C., 610
 Kozlik, F., 632
 Krabbé, K., 172
 Kreht, A., 203
 Kreilkamp and Boyden, 405
 Krogman, W. M., 647
 Krompecher, S., 637, 647, 649
 Kronfeld, R., 280
 Kubitschek, P. E., 85
 Kuehne, K., 74, 103
 Kunitomo, K., 105
 Kuntz, A., 171

- Labia majora*, 540, 541
 — *minora*, 541
Labial lamina, 267
Labyrinth, Evolution of, 322
 —, Ganglia of, 337
 —, Membranous, 332
Lachrymal bone, 292, 248
 — *canaliculi*, 313
 — *gland*, 313
Lacoste, A., 232
Lacroix, P., 647
Lacuna magna, 547
Lagena, 334
Lambda, 214
Lamina terminalis, 161, 173
Lamprey, Brain of, 156
Landau, E., 202, 203
Lander, K., 627, 631
Landra, G., 131
Langerhans, Islets of, 400
Langhan's cells, 20
Langworthy, O. R., 131
Lanugo, 651, 656
Larsell, O., 154, 294
Larynx, Evolution of, 490
 —, Functions of, 492
 —, Muscles of, 360, 492
 —, Sacculæ of, 493
Latarjet, M., 104
Lateral line, Organ of, 151, 322
Latissimo-condyloideus, 626
Lebedinsky, N. G., 85
Leboucq and Seydel, 232
Leche, Stella M., 75
Ledenyi, J., 474
Left-handedness, 70
Lens, Capsule of, 299
 —, Development of, 297
 —, Suspensory ligament of, 306
Leriche and Others, 647
Levander, G., 647
Levator ani, 571
 — *claviculae*, 626
Levi, G., 75, 475, 648
Levin, G., 203
Levin, P. M., 172
Lewinsky and Stewart, 280, 666
Lewis, F. T., 405, 425, 526
Lewis and Thyng, 425
Lewis, M. R., 590
Lewis, Sir T., 450
Lewis, W. H., 29, 64, 208, 217, 220, 299, 377, 475, 589, 590
Life periods of Primates, 85
Ligamentum teres, 635
Lightoller, G. S., 363
Lillie, F. R., 563
Limb bones, Differentiation of, 595
Limb-buds, 78, 574
 — *appear*, 26
 —, Experiments on, 69, 593
Limb, Differentiation of lower, 595, 596
Limb girdle, Rotation of, 597
Limbic bands, 449
Limbs, Congenital defects, 71, 73
 —, Development of, 592
 —, Differentiation of vessels, 596
 —, Evolution of, 592
 —, Malformation of, 594
 —, Morphology of, 599, 611
 —, Nerve supply of, 599
 —, Rotation of, 596
 —, Segmental nature of, 599
 —, Scheme of vessels, 606
 —, Superficial veins of, 608
Limson, M., 232
Linea alba, 580, 586
Lineback, P. E., 425, 610
Lindahl, Dr., 307
Lingual papillae, 367
 — *tonsils*, 371
Lingula, 221
Lip, Development of upper, 263
Lips, Development of, 238
 —, Evolution of, 256
 —, Separation of, 267
Littre, Glands of, 548
Liver, Blood-formation in, 469
 —, Divisions of, 385
 —, Development of, 383
 —, Growth of, 386
 —, Lobes of, 391
 —, Lobules of, 385
 —, Ligaments of, 388, 390
 —, Malformations of, 387
 —, Morphology of, 391
 —, Veins of, 385
Llorca, Orts, 30, 131, 442
Lloyd, L. W., 526
Lockhart, R. D., 264, 363
Lockhart and Brandt, 588, 590
Lockwood, C. B., 482, 563
Loewenthal, N., 320
Logan and Kronfeld, 280
Long and Zuckerman, 563
Longitudinal fissure, 174
 — *sinus*, Formation of, 201
Loosli, C. G., 498
Lorin-Epstein, M. J., 425
Low, A., 264, 385, 424, 600
Lower limb, Vessels of, 605
Lowsley, O. S., 550
Lucas, C., 527
Lucas, Clement, 246
Lucas Keene and Hewer, 405, 563
Lumbar curvature, 87
 — *fascia*, 577
Lunate sulcus, 190, 196
Lung buds, 480
Lungs, Adaptation to posture, 486
 —, Apices of, 484
 —, Blood supply of, 489
 —, Changes at birth, 490
 —, Growth of, 483, 485

- Lungs, Lobes of, 483, 486
—, Lymphatics of, 490
—, Modelling of, 484
—, Viable condition of, 484
Lymph sacs, 473
Lymphatic system, 471, 577
— nodes, 473
Lymphatics of lung, 490
— of mammae, 663
Lymphoblasts, 471
Lymphocytes, 470
Lymphoid tissue, Origin of, 370
Lynn, W. G., 74
- MacArthur, J. W., 74
MacConaill, M. A., 634, 647
MacGowan, T., 104
Mackenzie, Ivy, 321, 460
Macklin, C. C., 498
Macleod, J. A., 210
"
"
"
"
"
Malleus, 329
—, Formation of, 257
—, Origin of, 324
Mammae, Development of, 661
—, Evolution of, 659
Mammary remnants, 663
— ridge, 659
Mammillary processes, 100
Man, C., 631
Mandible, Development and ossification, 257
—, Evolution of, 258
—, Growth changes of, 258
Mandibular arch, Mesoderm of, 278
— cleft, 239
— condyle, Formation of, 257
— segment, 152
— process of face, 235
—, Parts formed in, 256
Mangold, H., 63
Mann, Ida, 294, 303, 320
Mann, T., 20
- Maxilla, First appearance of, 640
Marshal, F. H. A., 29
Marshall, Vein of, 431, 447
Marsupium, 554
Martin, C. P., 649
Martin, R., 103
Martinovitch, P. N., 75
Mastication, Apparatus of, 266
—, Muscles of, 252, 278, 360
- Mastoid, 335
— process, Evolution of, 220
Maturation of organs, 82
— tissues, 82
Maurer, H., 263
Maxillary antrum, 288
— process, 235, 249
—, Bones formed in, 251
—, Nerves of, 253
—, Parts derived from, 249
—, Vessels of, 253
— sinus, 254
—, Relation to molar-eruption, 255
— in apes, 256
Maxillo-turbinal, 248
Maximow, A., 590
Maxwell and Erwin, 459
McCown and Keith, 265, 280
McFeeters, J. W., 589
McGaw, W. H., 499
McGregor, A. L., 631
McIntyre, D., 48
McMurrich, J. P., 631
Meadley, J. C., 320
Measurement of embryo, 79
Mechanik, N., 459
Meckel's cartilage, 253, 256
— diverticulum, 409, 410
Meconium, 424
Median longitudinal bundle, 147
Medulla, Nerve centres of, 135
— oblongata, 133
Medullary canal, See Neural canal.
— folds, 23, 118
— laminae of hind-brain, 134
— plates, First appearance, 52
—, Origin of, 126
—, velum, Inferior, 138
—, Superior, 145
Medulloblasts, 121
Meibomian glands, 312, 659
Meiosis, 11
Melke, J., 48
Mellanby, Lady, 280
Membrana nictitans, 312
— tympani, 324, 325, 329, 331
Membrane bone, 211
"
"
"
"
"
Mercer, J., 631
Meredith, H. V., 85
Meredith, J., 631
Mesenchyme, 60
—, Definition, 589
Mesencephalon, See Mid-brain
Mesenteric arteries, 467
— recess, 389
Mesentery, Attachment of, 418, 423
—, Common genital, 3

- Mesentery, Dorsal, 381
 —, Primitive, 380
 —, Ventral, 381
 Mesocardia, 442, 465
 Mesoderm, Differentiation of, 59
 —, Origin of, 56
 —, Parts of, 25
 —, Segmentation of, 107
 Mesohepar, 388
 Mesogastrium, 393
 Mesoglia, 122
 Mesonephros, 501
 Mesorchium, 558
 Mesosalpinx, 3
 Mesovarium, 3
 Metacone, 280
 Metanephros, 501
 Metopic suture, 213
 Meyer, A. W., 474
 Meyer-Heydenhagen, G., 665
 Michels, N. A., 475
 Microcephaly, 216
 Microglia, 122
 Mid-Brain, I, 119, 146
 Mid-gut, 380, 408
 Migration of muscles, 625
 Mijsberg, W. A., 104, 233, 526, 527
 Miller, R. E., 74
 Miller, Ruth A., 609
 Miller, W. S., 498
 Miller and Detwiler, 609
 Minear, W. L., 378
 Minnett, F. C., 264
 Mirror-image theory, 630
 Mitchell, G. A. G., 527, 563
 Moellendorf, W., 475
 Moeller-Holst, G., 320
 Molar teeth, 273
 — —, Extra, 277
 Mole, Production of, 65
 Monocytes, 470
 Monsters, Double, 65
 Mons veneris, 542
 Montagu, M. F. Ashley, 232, 243, 264
 Monteiro and Carvalho, 649
 Moore, C. A., 563
 Moore, R. A., 550
 Mortimer, H., 232, 647
 Morton, Dudley J., 631
 Morula, 13
 Mossman, H. W., 48
 Moszkowicz, L., 553, 562
 Mouth, Formation of, 379
 Movements of foetus, 123
 Müller, Charlotte, 584, 590
 Müller, Fibres of, 303
 Müller, J. H., 526
 Müllerian bulb, 517
 — ducts, 515, 505
 — — in male, 523
 Müller's muscle, 309
 Mummery, J. H., 279
 Murotori, G., 30, 75
 Murray, P. D. F., 69, 609, 646, 654, 666
 Muscle, Renewal of in heart, 457
 — fibres, Development of, 588
 — —, Formation of, 108
 — spindles, 588
 — striation, 589
 Muscles, Anomalies of, 626
 —, Migration of, 109, 625
 —, Of body wall, 586
 —, Of hand and foot, 625
 —, Of mastication, 278
 —, Segmental, 108
 Myelinization of tracts, 126
 Myeloblast, 470
 Myelospongium, 121
 Myerson, M. C., 293
 Myoblasts, 109, 588
 Myopia, 310
 Myosyneptium, 108
 Nails, 657
 Nares, Atresia of, 251
 Nasal bones, 258
 — Cavities, Development of, 282
 — —, Evolution of, 282
 — —, Expansion of, 286
 — —, Formation of, 236
 — duct, 246, 291
 — oclusions, 293
 — processes, 283
 — —, Structures formed in, 231
 — septum, 241
 — —, Growth of, 250
 — —, Origin of, 219
 — sinuses, 286
 — turbinates, vestigial, 290
 Nasion, 227
 Nasmyth's membrane, 270
 Naso-palatine foramen, 246
 Naso-turbinal, 290
 Nayak, U. V., 631
 Neck, Displacement of vessels, 360
 —, Evolution of, 343, 464
 —, Formation of, 362
 Needham, J., 29, 48, 62, 73, 103, 104, 320, 563, 609
 Needles, J. H., 131
 Negus, V., 377, 378, 499
 Nehse, E., 665
 Nelson, W. O., 172, 666
 Neocortex, 170
 Neocranium, 231
 Neopallium, Evolution of, 187
 Nephric duct, 501
 — tubule, 500
 Nephrocele, 500
 Nephrogenic cord, 505, 510
 Nephron, 512, 527
 Nerve cells, Origin of, 126
 — fibres, Growth of, 69

Nerve fibres, Growth cones of, 129
 — —, Guidance during development, 605
 — plexuses, Formation of, 603
 — sheaths, Development of, 130
 — supply to muscles, 605
 Nerves, Communications between median and ulnar, 603
 —, Development of, 129
 — of lower limb, 603
 — of orbit, 313
 — of pharyngeal region, 353
 —, Segmental, 110
 —, Somatic, 111
 —, Splanchnic, 111
 Nervous system, Evolution of, 117
 Nervus bigeminus, 604
 — furcalis, 604
 — terminalis, 291
 Neural arch, 93
 — canal, 117
 —, Formation of, 24
 — crest, 111
 — — in head region, 150
 —, Derivatives of, 128, 130
 Neurenteric canal, 22
 — — — — —
 — — — — —
 — — — — —
 — — — — —
 — of cord, 126
 Neuron, defined, 127
 — theory, 130
 Neuropore, Anterior, 159
 Neuropores, 118
 Neuters, 68
 Newman, H. H., 67, 665
 Ngowyang, G., 203
 Nicholas, J., 609, 610
 Nicholson, C., 589, 630
 Nicholson, G. W., 73, 378, 425, 564, 649
 Nicol, T., 48, 425
 Nipple, Development of, 660
 Noback and Rehman, 474
 Noel and Pigeaud, 527
 Nonidez, J. F., 132, 363
 Norberg, O., 244, 264
 Norris, E. H., 378
 Nose and eye compared, 286
 — See also under Nasal.
 —, Malformations of, 292
 —, Duplication of, 240
 —, Meatuses of, 287
 —, Vessels of, 248
 Notochordal plate, 52
 Notochord as evocator, 92
 —, Development of, 52
 —, Fate of, 91
 —, First appearance of, 51
 —, Formation of, 25, 91

Notochord, Origin of, 60
 —, Organizing properties of, 64
 Nucleus pallidum, 179
 Nutrient vessels, 641
 Nylander, E. S., 631
 Oblique vein, 432
 O'Brien, H. D., 405
 Obturator nerve, 605
 — fascia, 575
 Occipital bone, Ossification of, 212, 217, 218
 — —, Formation of, 216
 — condyle, median, 98
 — condyles, 218
 — cortex, 317
 — fontanelle, 218
 — lobe, 317
 — —, fissures of, 197
 — ridges, 229
 — somites, 97
 Occipito-Cervical somites, 97
 — — variations, 91
 O'Connell, J. E. A., 204
 O'Connor, R. J., 514, 526
 Ocular axis, 309, 313
 Oculo-motor nerve, 152
 Odgers, P. N. B., 30, 48, 104, 405, 425, 459, 460
 Odontoblasts, 270
 Odontoid of atlas, 92
 Odontomes, 270
 Oesophagus, 382, 480
 —, Malformations of, 382,
 Oestrin, 7, 31
 —, Action of, 521, 525, 660
 Oestrogen, 553, 561
 —, Action in foetus, 527
 —, — on pelvis, 613, 614
 Oestrone, 67
 Oestrus, 28
 Oettinger, B., 648
 Ogawa, C., 342
 Okkels, H., 527
 Olfactory bulb, 284
 — epithelium, 283
 — nerves, 283
 — pits, 283
 — plaques, 282
 — structures, 282
 — tracts, 286
 Oligodendroglia, 122
 Oliva, M. de, 341
 Ovary bodies, Origin of, 136
 Omentum, great, 402
 Omo-sternum, 583
 Omo-vertebral bone, 611
 Opercula of island of Reil, 194
 Opisthon, 227
 Optic cup, 299
 — —, Organizing properties of, 64

- Optic nerve, Development of, 300
 — radiations, 317
 — thalamus, 159, 180
 — —, Projection of fibres to cortex, 202
 — tracts, 300, 315
 — vesicles, 118, 158
 — —, Structures formed from, 299
 Oral plate, 165, 262
 Orbit, Formation of, 310
 Orbital region of skull, 209
 Orbito-sphenoid, 219
 Organizers, 63
 Organ of lateral line, 151
 Orthograde posture, 86, 566
 Orts, L. F., 459
 Os acetabuli, 613
 — anti-epilepticum, 223
 — centrale, 619
 —, Incac, 224
 — trigonum, 618
 — styloideum, 620
 Ossification of spine, 96
 Osteoblasts, 636
 —, Control of by hormones, 642
 Osteoclasts, 638
 Otic capsule, 206
 Otocephaly, 70
 Otocyst, 322
 —, Developmental powers of, 340
 Otoliths, 332
 Ova, Discharge of, 6
 —, Implantations of, 15
 —, Origin of, 26
 Ovarian follicles, 7
 Ovario-pelvic ligament, 552
 Ovario-testis, 68, 559
 Ovary, Descent of, 2
 —, Foetal, 2
 —, Position of, 4
 —, Round ligament of, 3
 Ovum, Culture of, 69
 —, Descent to uterine cavity, 8
 —, Division of 9
 —, Fertilization of, 8
 —, Formation of, 5
 —, Implantation of, 32
 — of marsupials, 40
 —, Size of, 1
 —, Structure of, 9

 Pain, referred, 113
 Palatal folds, 251
 — process, 249
 — rugae, 25
 Palate, Cleft, 238
 —, Development of, 250
 —, Malformations of, 250
 — of foetus, 226
 —, Primitive, 234
 Palato-quadrate, 220
 — bar, 238, 233, 252

 Paleoecranium, 231
 Pallium. See under cerebral cortex.
 Palm, Lines of, 654
 Palmar fascia, 577
 Palmaris longus, 627
 Palmer, D. W., 498, 499
 Pan, M., 459
 Pancreas, Development of, 398
 —, Ducts of, 399
 Pankratz, O. S., 563
 Papanicolaou, G. N., 48
 Papez, J. W., 171, 342, 425, 426
 Papillae foliatae, 367
 Papillary patterns, 563
 Parachordal cartilages, 92, 216
 Paracone, 280
 Paradidymis, 508
 Paraflocculus, 144
 Paraganglia, 356, 562
 Parallel fissure, 199
 Para-mastoid process, 229
 Paramore, R. H., 572, 589
 Para-occipital process, 228
 Parapineal, 172
 Paraseptal cartilages, 241
 Paraterminal body, 182, 187, 285
 Parathyroids, 372, 377, 374
 Paraxial mesoderm, 25, 59
 Parietal bone, 211
 — —, Ossification of, 213
 — foramen, 214
 Parkes, A. S., 549
 Paroophoron, 507
 Parotid gland, 368
 Parovarium, 507
 Pars membranacea septi, 457
 Parsons, F. G., 265, 352, 362, 462, 580,
 598, 647, 648
 Pars triangularis, 193
 Partridge, E., 631
 Pasteels, J., 61
 Patella, 644
 —, Anomalies of, 648
 Paterson, A. M., 579, 585, 590
 Paterson, R. S., 648
 Patje, A., 630
 Patten, B. M., 460
 Patten, C. H., 232
 Patten and Kramer, 459
 Patzelt, V., 404, 425
 Paulet, J. L., 240, 377
 Payton, C. G., 614, 630, 640, 647, 648
 Pearson, A. A., 155, 294, 362
 Pearson and Davin, 648
 Pectoralis externus, 627
 — minor, 627
 Pei-lin Li, 425
 Pelvic bar, 613
 — colon, 415
 — fascia, 572, 575
 — floor, 566, 569
 — girdle, 582, 612

- Pelvis, Form of, 568
 —, Growth of, 614
 Penis, Development of, 538
 —, Evolution of, 529
 Penrose, L. S., 561, 665
 Pericardium, 465
 —, Separation of, 431
 Perichondrium, 633
 Pericranium, 214
 Periderm, 650
 Peridontal membrane, 271
 Perilymph system, 335
 Perineal muscles, 543
 — raphe, 540
 Perineum, Formation of, 636
 Periotie capsule, 323
 — —, Development of, 334
 Peristalsis, 424
 Peritoneal adhesions, 407
 — cavity, Origin of, 381
 — funnel, 500
 Peritoneum, Lesser sac of, 403
 Pernkoff, E., 404, 425
 Pernkopf and Wirtinger, 460
 Peroneus quinti digiti, 625
 — tertius, 622
 Personen, N., 649
 Peter, K., 154, 263
 Peter's embryo, 18
 Peters, H. B., 233
 Petro-mastoid, 218
 —, Ossification of, 335
 Petro-aquamosal suture, 213
 Pfeiffer, C. A., 29
 Pfitzner, W., 531
 Phalanges, Differentiation of, 596, 623
 —, Ossification of terminal, 658
 Phallic groove, 539
 Pharyngeal recesses, 347, 370
 — tonsil, 369
 Pharynx, Early development, 343
 —, Evolution of, 343
 —, Lateral recess of, 350
 — of embryo, 344
 Phelps-Allis, E., 172
 Phenotype, 68
 Phosphatase, 643
 Pia mater, Origin of, 128
 Pincus, G. G., 29
 Pinal body, 167
 — —, Development of, 168
 — —, Tumours of, 169
 — eye, 167
 — striae, 167
 Pinna, Muscles of, 326
 Pires de Lima, 527, 610
 Pisiform, 620
 Pittard, E., 85
 Pittard and Kaufmann, 232
 Pituitary, Hormones of, 7
 — body, 164
 — —, Circulation of, 166
 Pituitary body, Development of, 160
 — —, Nerve supply of, 162
 — —, Pharyngeal remnants, 166
 — —, Position of, 222
 Placenta, bidiscoidal, 44
 —, Formation of, 43
 —, Structure of, 46
 Placental blood-spaces, 20, 41
 — circulation, 41, 46
 Placodes, epi-branchial, 348
 Plantar fascia, 577
 — ligaments, 624
 Plantaris, 627
 Plantigrade posture, 566
 Platt, H., 630
 Platycnemias, 646
 Platymeria, 646
 Platysma, Origin of, 360
 Pleurae, 482
 Pleural cavities, Evolution of, 478
 — passage, 478, 482
 Pleuro-peritoneal folds, 494
 — opening, 493, 496
 — passage, 381
 Plica gubernatrix, 552
 — semilunaris, 312, 371
 — triangularis, 371
 — vascularis, 3, 352
 Plicae fimbriatae, 367
 Pohlman, A. G., 549
 Polar bodies, 9
 — cartilages, 232
 Politzer, G., 294, 378, 540, 563
 Politzer and Hann, 378
 Pollex, Muscles of, 624
 Pons, Transverse fibres of, 143
 Pons-Tortella, E., 264, 377
 Pontine flexure, 138, 148
 Popa and Fielding, 172
 Popliteus muscle, 635
 Popper, R., 549
 Portal vein, Origin of, 435
 Posener and Others, 648
 Post-frontal, 224
 Post-orbital process, 600
 Poynter, C. W. M., 459
 Prechordal plate, 53
 — region of cranium, 206
 Pre-chorion, 44
 Pre-coracoid, 615
 Pre-mandibular segment, 153
 Premature births, 82
 Pre-maxilla, 242
 —, Ossification of, 242
 —, Relationship to clefts, 245
 —, Relations to maxilla, 243, 264
 Prepuce, 540
 Preputial glands, 548

- Presumptive ectoderm, 64
 Preto, V., 405
 Prevertebral ganglia, 112
 Price, Dorothy, 550
 Priman, J., 527
 Primates, Life periods of, 85
 Primitive germ cells, 26
 — node, 22, 53, 57
 — streak, 21, 50
 — —, Later history of, 55
 — —, Organizing properties of, 63
 Primordial ova, 5, 26
 Pritchard, J. J., 647
 Processus hypochiasmata, 220
 — vaginalis, 556
 Progesterone, 7, 31
 Prolactin, 660
 Pronephros, 501, 505
 Pronograde posture, 86
 Pronucleus, Female, 9
 —, Male, 13
 Prosencephalon. See fore-brain.
 Prostate, 545
 —, Enlargement of, 547
 —, Influence of hormones on, 547
 —, Nature of, 547
 Prosthion, 227
 Protocone, 280
 Protopathic theory, 114
 Protovertebrae or somites, 93
 Pryor, J. W., 74, 641, 648
 Psoas parvus, 629
 Pterion, 214
 Pterygoid muscles, 278
 — plates, 221, 252
 Pubic apron, 553
 — hair, 656
 Pubis, 613
 Pubo-prostatic ligament, 576
 Puiggros-Sala, J., 498
 Pulmonary arteries, 357
 — circulation, 429
 — pocket, 480
 — system, 461
 — —, Evolution of, 467
 — veins, 451
 — vessels, 489
 Pulp of teeth, 270
 Pupillary membrane, 306
 Purkinje cells, 141
 — system, 461
 Pyramidal tracts, 125
 Pyramidalis, 628
 Pyriform fossa, 350
 — lobe, 182

 Quadrangle bone, 253
 Quadratus lumborum, 496
 Quadrigeminal plate. See Tectum
 Quadruplets, 67
 Quelprud, T., 342
 Quickening, 79

 Rachischisis, 127
 Radslob, E., 320
 Rami communicantes, 112
 Ramsay, A. J., 378
 Ramsey, E., 30, 48
 Ransom and Others, 362
 Rathke's pocket, 165, 261
 Raven, C. P., 132
 Ray, Evans and Becks, 648
 Reagan F., 342, 363
 Recapitulation, 315
 —, Law of, 50
 Receptaculum chyli, 473
 Receptor mechanism in straight sinus, 169
 Recto-vesical fascia, 575
 Rectum, 414
 —, Malformations of, 536
 —, Migration of termination, 535
 —, Muscles of, 545
 Rectus abdominis, 109, 587
 — —, Segmentation of, 590
 Red nucleus, 147
 Reagan and Wilkins, 647
 Reesc, A. M., 263
 Reid, D. G., 425
 Reid, R. W., 131
 Reider, N., 425
 Reissner's fibre, 148
 — membrane, 337
 Remane, A., 280
 Renal agenesis, 515
 — tubules, Experiments on, 65
 — vessels, 110
 Respiration, Mechanism of, 493
 —, Muscles of, 565
 Respiratory system, 476
 — —, Development of, 480
 — —, Morphological parts of, 479
 Retactor ani, 570
 Rete testis, 509
 Retina, Ciliary part of, 300
 —, Development of, 302
 —, Nerve elements of, 127
 —, Pigmentary layer, 300
 Retropharyngeal diverticula, 377, 382
 Retzius, G., 665
 Reynolds, R. J., 105, 589
 Rhesus monkey, Blastocysts of, 15
 Rhinencephalon, 285
 Rhombic lip, 138
 Ribs, bicapital, 80
 —, cervical, 90
 —, Development of, 95, 99
 —, Sternal, 582
 —, Formation of, 580
 —, Vestigial, 99
 Riches and Muir, 550
 Richter, W., 665
 Riddle, O., 666
 Riddoch, G., 171
 Riedel's lobe, 393

Ries and Langworth, 171
 Rittmeister, J. F., 665
 Roberts, J. A. F., 29, 74
 Roberts and Greenwood, 563
 Robinson, A., 320, 428
 Robinson and Best, 648
 Robison, R., 648
 Robson, J. M., 47
 Rogers, L., 378
 Rogers and West, 154
 Romanes, G. J., 131, 362
 Romer, A. S., 630
 Rondolini, G., 474
 Roper-Hall, H. T., 294
 Ropes, M. W., 498
 Rosenberg, E., 89, 104
 Rosenmüller, Fossa of, 350
 —, Organ of, 607
 Rosenthal, A. F., 404
 Rosenthal and Willis, 564
 Rossman, I., 48
 Rottter, H., 459
 Rubashkin, W., 377
 Ruggles, G., 648
 Ruth, E. B., 630
 Rutherford, A. H., 425
 Rutherford, N. C., 630

Sabin, Florence, 471, 475
 Sacral plexus, 601
 Sacro-coccygeal junction, 89
 — iliac joint, 613
 — lumbar junction, 89
 — sciatic ligament, 572
 Sacrum, 89
 —, Morphology, 100
 Sagittal fontanelle, 214
 Salivary glands, Origin of, 368
 Salmon and Dor, 459
 Salisbury, C. R., 589
 Sanabria, T., 460
 Santo, E., 646
 Santorini, Cartilage of, 492
 Saphenous artery, 607
 — nerve, 605
 — veins, 608
 Sancer, F. C., 131
 Sauser, G., 104
 Scala tympani, 335
 — vestibuli, 335
 Scalkunow, S., 475
 Scalp, Capillary plexus of, 254
 Scammon, R. E., 85, 405, 648
 Scammon and Norris, 459
 Scansorius, 629
 Scaphocephaly, 226
 Scapula, 598
 —, Congenital elevation of, 102
 Schaeffer, J. P., 264, 294
 Schaeuble, J., 665
 Schaffer, J., 377

Schapschal, J., 425
 Scharpenberg and Windle, 131
 Scharrer, E., 171
 Schepers, G. W. H., 202, 204
 Schmidt, C. A., 343
 Schimert, J., 342, 362
 Schneider, A. J., 155
 Schneider, H., 404
 Schneider, P. P., 293
 Schoenherr, H., 665
 Schour, I., 280
 Schroeder, C. H., 263
 Schroeter, H., 527
 Schultz, A. H., 48, 85, 104, 232, 280, 563,
 590, 631, 648, 655, 665
 Schwalbe, E., 74
 Schwann, Cells of, 130
 Schwartz, H. G., 172
 Schwegler and Boyden, 405
 Schwyzer and De Garis, 610
 Sciatic nerve, Division of, 604
 Sclerotic, 308
 Sclerotomes, 91
 Scott, G. H., 405
 Scott, J. P., 341
 Scrotum, 640, 643, 554
 Schreiner, J., 650

Scevers, C. H., 626
 Segment, Constitution of, 107
 Segmental vessels, 109
 Segmentation, 23
 —, Irregularities of, 101
 — of body, 106, 679
 — of brain, 149
 — of cranium, 206
 — of Embryo, 60
 — of head, 62, 149, 229
 — of mesoderm, 91, 93
 —, Neighbouring segments affected, 280
 —, Note on, 103
 Segments connected with eye, 314
 — in limbs, 599
 —, Nerves of, 110
 Seib, G. A., 459, 631, 632
 Selachian skull, 208
 Seligman, S. B., 630
 Selye, H., 647
 Selye and Schenker, 475
 Semilunar cartilages, 636
 Seminal guides, 533
 Seminaliferous tubules, 552
 Senior, H. D., 605, 610
 Sense organs, 664
 Septa, intersegmental, 108
 Septum of nose, 241
 — lachrym, 188
 — primum, 452
 — secundum, 453
 — transversum, 381, 384

- Septum transversum, Migration of, 431
 Sertoli cells, 12
 Sesamoid, ossifications, 644
 Sesamoids, 629
 Sex, Change of, 67
 — differentiation, 518, 553, 559, 560
 —, Determination of, 27, 67
 —, Hormone control of, 67
 —, Imperfect, 559
 —, Intermediate, 67
 —, when distinguishable, 80
 Sex-linked-malformation, 614
 Sgalitzer, K. E., 378
 Shafik, A., 172, 321, 377
 Shaner, R. F., 202, 362, 460, 474
 Shanklin, W. M., 172
 Shaw, D. Batty, 666
 Shaw, J. C., 280
 Shaw, W., 74
 Sheath cells, 121
 Sheehan, D., 116
 Sheehan and Others, 363
 Sheldon and Ogilvie, 404
 Shellshear, J., 202, 203, 204, 321
 Sheppard, E. M., 75
 Sherrington, Sir C., 588, 602, 605
 Shikinami, J., 526, 549
 Shore, L. R., 104, 475, 527, 610
 Shoulder, Congenital elevation of, 611
 — girdle, 582, 615
 Siamese twins, 66
 Siddiqui, M., 74
 Siddiqui and Mullick, 115
 Sidhom and Derry, 648
 Sight, Nerve centres and structures, 315
 —, — structures of, 319
 —, Structures connected with, 295
 Sigmoid colon, 415
 Silvestri, U., 549
 Simian fissure, 196
 Simkins, C. S., 28, 526, 562
 Simmons and Todd, 85
 Sino-aortic node, 449
 Sinus pocularis, 523
 — subpericardiacus, 489
 — venosus, 445
 —, Fate of, 446
 Sitarama, Rao, V., 131
 Sitsen, A. E., 232
 Sive, S. A., 405
 Skene's tubules, 546
 Skerlj, B., 85
 Skin and its Appendages, 650
 —, Development of, 651
 —, Evolution of, 650
 —, Strata of, 652
 Skull. See also under cranium.
 —, Base of, 206
 —, Development of, 211
 —, Segmentation of, 229
 Skulls, Aeromegalic, 226
 Slonimski, P., 475
 Smith, Ross, 610
 Smith, Sydney, 264
 Smith and Boulgakow, 610
 Snook, Thomas, 369, 378
 Solitary tract, 136
 Solnitzky, O., 405
 Somatic nerves, 111
 — motor centres, 135
 Somatopleure in chick, 39
 —, 25, 59
 Somite. See also under segment.
 Somites, 93
 —, Formation of, 23, 26, 60
 — of head, 149
 Spanner, R., 46, 475
 Spaulding, M. H., 549
 Speert, H., 666
 Speidel, C. C., 75, 115, 132, 590
 Spemann, Hans, 63, 69, 73
 Spermatocytes, 12
 Spermatozoa, Formation of 12
 —, Origin of, 26
 Sphenoid, Development of, 219
 —, Elements of, 207
 Sphenoidal fissure, 220
 — sinus, 289
 — turbinate, 221
 Sphincter colli, 361
 — of iris, 308
 — of Oddi, 400
 Spiegel, E., 172
 Spiegelian lobe, 391
 Spina bifida, 127
 Spinal accessory, 354
 — cord, 119
 —, Connection of nerves with, 112
 —, Differentiation of, 120
 —, Grouping of cells, 122
 —, Malformations of, 127
 —, Membranes of, 128
 —, Segmentation of, 111, 114, 126
 —, Shortening of, 10
 —, Vessels of,
 — column, Curves of, 87
 —, Development of, 86
 —, Evolution of, 86
 —, Evolution of, 86
 —, Variations of, 87
 — tracts, Development of, 124
 Spine, Curves of in embryo, 80
 —, Lumbar elongation, 513
 —, Ossification of, 96
 —, Proportions of bone and cartilage, 87
 —, Pyramids of, 87
 —, Unstable regions of, 87
 Spinous processes of vertebrae, 100
 Spirow, M., 131
 Spitzer, A., 62, 460
 Splanchnic fibres, Emergence of, 114
 — motor centres, 135
 — nerves, 111
 Splanchnopleure, 25, 59

Spleen, Blood-formation in, 469
 —, Development of, 396
 —, Ligaments of, 398
 Spondylolisthesis, 101
 Sprawson, E., 280
 Sprengel's shoulder, 630
 Sprengel, H. B., 280
 Squamosal bone, 212
 Stacey, R. S., 649
 Stallworthy, J. A., 232
 Stamm, T. T., 631
 Stanley, H. S., 563
 Stapes, 329
 —, Origin of, 324
 Starkie & Stewart, 281
 Stature, Increase of, 83
 Stearns, Mary L., 590
 Steiner, K., 665
 Stengel, F., 404
 Stern, K., 203
 Sternalis muscle, 495, 587, 627
 Sternal-clavicular fibrocartilage, 634
 — manubrial joint, 580
 — mastoid, 627
 Sternum, 581
 —, Development of, 583
 —, Morphology of, 582
 —, Ossification, 586
 Stewart, T. D., 104, 630
 Stewart, D., 649
 Stibbe, E. P., 320
 Stieda, L., 665
 Stieve, H., 30, 49, 562
 Stockard, C. R., 74
 Stoehr, P., 132, 363
 Stomach, Development of coats, 395
 —, Rotation of, 394
 Stomodaeum, 105, 235, 256
 —, Fate of, 261
 Stopford, Sir, J., 114, 154, 321
 Strangways and Fell, 69, 320, 648
 Straus, W. L., 527, 631
 Streeter, G. L., 15, 30, 48, 56, 61, 71, 105,
 131, 204, 333, 338, 353, 601, 609
 —, —, Age of embryos, 84
 —, —, On ear, 341
 Striae vasculares, 337
 Striate cortex, 196
 Stricht, O., van der, 342
 Strukow, A. I., 498
 Struthers, Ligament of, 626
 Stylo-hyal, 351
 Stylo-mandibular ligament, 368
 Subarachnoid spaces, 139, 202
 Subarcuate gyrus, 188
 Subcardinal veins, 434
 Subclavian arteries, 353, 467
 —, —, Abnormalities of, 359
 — vein, 433
 Subcommissural organ, 149
 Sub-dural space, 202
 Submaxillary gland, 368

Subperitoneal tissue, Plasticity of, 518
Subthalamus, 171
Subvertebral muscles, 496
Suk, V., 642
Sulcus terminalis of tongue, 366
Sunderland, S., 172, 203, 204
Supracallosal gyrus, 188
Supracardinal vein^s, 434
Supra-condylar process, 630
Supragranular cortex, 189
Supra-occipital, 224
Suprarenal, See Adrenal,
Supra-scapula, 615
Supra-sternal bones, 615
Supra-sternals, 583
Sutures, Closure of, 213
—, Premature closure of, 216
— of skull, Formation of, 214
Sverdrup, A., 610
Swale-Vincent and Curtiss, 564

Symphysis pubis, 613
Sympodia, 608
Syncytium, 20, 33
Syndactyly, 608
Synovial membrane, 633
Szepsenwol, J., 475
Szymonowicz, G., 660

Tail, Development of, 101
—, Muscles of, 571, 628
—, Recession of, 79
—, Vestiges of, 570
— gut, 531
Tamura, O., 460
Tapetum lucidum, 309
Tarkhan, A. A., 155, 321
Tarsus and carpus compared, 618
—, Anomalous associations of, 621
Taste buds, 367
Taurodont teeth, 276
Tawara, 461
Tectorial membrane, 337
Tectum, 147, 171, 315
— of chondrocranium, 207
Teeth, 266
— See also under dentition.
—, Dates of formation, 273
—, Effects of civilization on, 278
—, Eruption of, 276
—, — of upper molars, 255
—, Evolution of, 268
—, Germination of, 276
—, Growth movements of, 277
—, Morphology of, 274
—, Nomenclature of cusps, 280

- Teeth, Roots of, 276
 —, Structure of, 268
 —, Supernumerary, 277
 —, Tritubercular, 275
 —, Vestigial, 267
 Tegmen tympani, 328
 Tela choroidea, 153
 Telencephalon, 158
 Temporal ridges, Upgrowth of, 229
 Temporo-mandibular articulation, 209,
 253, 258, 259, 634, 647
 Tench, E. M., 549
 Tendon fibres, 588
 Tenon, Capsule of, 309
 Tensor tympani, 328
 Tentorium cerebelli, 148
 Teratology, Definition of, 73
 —, Literature of, 74
 Teratomata, 27
 —, Origin of, 64
 Testis, Attachments of, 551
 —, Cause of descent, 557
 —, Descent of, 555
 —, Ectopic position of, 556
 Testosterone, 67
 Teixeira, C., 649
 Thalamencephalon, 157
 Thalamus, Literature on, 171
 Thebesian valve, 448
 Thompson, J. M., 203
 Thompson, I. MacLaren, 405, 609
 Thompson, P., 24, 589
 Thompson, R., 549
 Thomson, Arthur, 225, 233, 265, 405
 Thoracic duct, 473
 Thorax, Postural modifications of, 566
 —, Shape of, 488
 Thumb. See Pollex.
 Thurnesse, A., 590
 Thymus, 371
 Thyro-glossal duct, 375
 Thyroid, aberrant, 375
 — cartilage, 352, 491
 —, Development of, 374
 —, Origin of lateral lobes, 378
 Tibialis posticus, 624
 Tiegs, O. W., 280, 591
 Tilney, F., 164, 202
 Todd, T. Wingate, 82, 85, 90, 104, 232,
 265, 613, 630, 647
 Todd and Lyon, Closure of sutures, 321
 Todd and Tracey, 232
 Todd and Wharton, 233
 Toenbury, G., 424
 Tomes' fibres, 270
 Tongue, Abnormalities of, 366
 —, Development of, 364
 —, Muscles of, 366
 —, Nerves of, 365
 Tonsil, Development of, 370
 —, Pharyngeal, 368
 Toro, E., 647
 Touch bodies, 664
 Tower, Sarah S., 649
 Trabeculae cranii, 218
 Trachea, 491
 —, Development of, 480
 Transplantation of tissues, 64
 Transposition of parts, 69
 Transverse vertebral processes, 100
 Trapezius, 109, 360, 627
 Traut, H. F., 527
 Tredgold, A. F., 590
 Treitz, Muscle of, 409, 413
 Triangular fibro-cartilage, 634
 — ligament, 575
 Triplets, 67
 Trochanter, third, 644
 Troitzky, W., 233
 Trophoblast, 16, 20
 Trotter, M., 630
 Trotter and Dawson, 665
 Truncus arteriosus, 445, 453
 Tubal pregnancy, 9, 20
 Tuberculum impar, 364
 Turbinate processes, 248, 287
 Turyna, E., 363
 Twins, Identical, 67
 —, Parabiatic, 67
 —, Production of, 65
 Twisselmann, F., 62
 Tympanic bulla, 329
 — plate, 259, 325
 — ring, 260
 Tympano-hyal, 351
 Tympanum, 328
 —, Attic of, 329
 Tyson's glands, 548
 Ultimo-branchial body, 375, 376
 Umbilical artery, 466
 — coelum, 409
 — cord, Formation of, 42
 — hernia, 411
 — veins, 385, 438
 — vessels, Evolution of, 38
 Umbilicus, Changing state of, 579
 —, Weeping patch, 411
 Union of parts, 240
 Uotila, U. U., 563
 Upham and Landauer, 665
 Urachal cysts, 544
 Urachus, 544
 Ureter, 410
 Urethra, Formation of, 549
 —, Muscles of, 545
 Urogenital mesentery, 505
 — sinus, 521, 524, 532
 — system, Evolution of, 500
 Urorectal septum, 538
 Uterus, 515, 518
 —, Malformations of, 519
 —, Musculature, of, 519

- Uterus, Round ligament of, 3, 518
 Utricle, 334

 Vagina, Atresia of, 521
 —, Formation of, 518
 —, Metamorphosis of, 521
 Vagus, 153, 353
 Vandebroek, G., 61
 Van Dyke, J. H., 378
 Variations. See under each structure.
 Variot and Cotcu, 103
 Vas aberrans, 607
 Vasa aberrantia, 508
 — efferentia, 508
 Vaso-motor nerves, 112
 Vaterian ampulla, 399
 Veau and Politzer, 237, 262
 Veau, V., 262
 Veins, Superficial of limbs, 608
 Velum interpositum, 174, 175
 Vena cava, inferior, Origin of, 429, 434
 — — superior, 429
 Venous sinuses of brain, Development of, 200
 — valves, 446
 Ventral median line, 578
 Ventricle, 4th, 134
 Ventricles, Development of, 450
 Vento-lateral musculature, 108
 Verhaart and Kennard, 203
 Vernix caseosa, 639
 Vertebra, Parts of, 93
 —, Development of, 94
 —, Ossification of, 95
 Vertebral column, Early evolution of, 161
 — column. See also spinal column and spine.
 Vesalius, Bone of, 621
 Vessels, segmental, 109
 Vestibular ganglion, 337
 — nuclei, 141, 340
 Vestibule, 335
 Vestigial muscles, 626
 Vibrissae of wrist, 635
 Vilas, E., 527
 Villi, Placental, 20
 Viscera, Transposition of, 69
 Visceral arches and grooves, 345
 — —, Arteries of, 356
 — —, Cartilages of, 351
 — —, Muscles of, 360
 — —, Nerves of, 353
 — —. See also under branchial.
 — recesses, 349

 Wade, H. J., 172
 Waddell, G., 362
 Waddington, C. H., 29, 30, 75
 Wagenen, G., van, 550
 Waheed, A., 85
 Wakeley, C. P. G., 104, 105, 363, 425, 426, 549, 610
 Wakeley and Edgeworth, 362
 Walker, A. E., 171, 342
 Walking, When begun, 103
 Wallart, J., 626
 Wallis, Ruth, 641, 648
 Walls, E. W., 462, 474
 Walmsley, R., 460, 590, 646
 Walmsley, T., 116, 425, 460, 647
 Walmsley and Bruce, 647
 Waterman, A. J., 425
 Watson, D. M. S., 609, 630
 Watt, J. C., 126, 204, 459
 Watts, J. W., 204
 Wax glands, 659
 Webb, R. L., 475
 Weber, F. P., 131
 Weddell, G., 115, 648
 Weddell and Others, 377
 Weddell and Posener, 131
 Weed, L. H., 204
 Weekes, H. C., 48
 Weller, G. L., 378
 Wells, L. H., 563
 Weidenreich, F., 232, 265
 Weinberg, E., 626
 Weinert, H., 589
 Weiss, Paul, 131, 154, 610
 Weissberg, H., 405, 425
 West, C. M., 30, 65, 155, 264, 266, 279, 378
 Weston, Jean, K., 342
 Wharton's jelly, 43
 Wherry and Anson, 264, 279
 Whillis, J., 636, 646
 White, E. G., 404
 Whitehead, R., 563
 Whitehead and Waddell, 590
 Whitnall, S. E., 309, 320
 Whitnall and Beattie, 320
 Wierda, J. L., 425
 Wilder, H. H., 665
 Williams, G. A., 631
 Williams, J. W., 49
 Williams and Cunningham, 563
 Williams and Edmonds, 363
 Williamson, G. S., 378
 Wilber, B. H., 30
 Wilks, R. A., 74, 666
 Wilson, H. G., 493
 Wilson, J. T., 154
 Wilson, K. M., 526, 549, 562
 Winckler, G., 115, 320
 Windle, W. F., 154, 363
 Windle and Fitzgerald, 84, 131
 Wintrobe and Schumacker, 475

- Teeth, Roots of, 276
 —, Structure of, 268
 —, Supernumerary, 277
 —, Tritubercular, 275
 —, Vestigial, 267
 Tegmen tympani, 328
 Tela choroidea, 153
 Telencephalon, 158
 Temporal ridges, Upgrowth of, 229
 Temporo-mandibular articulation, 209,
 253, 258, 259, 634, 647
 Tench, E. M., 549
 Tendon fibres, 588
 Tenon, Capsule of, 309
 Tensor tympani, 328
 Tentorium cerebelli, 148
 Teratology, Definition of, 73
 —, Literature of, 74
 Teratomata, 27
 —, Origin of, 64
 Testis, Attachments of, 551
 —, Cause of descent, 557
 —, Descent of, 555
 —, Ectopic position of, 556
 Testosterone, 67
 Teixeira, C., 649
 Thalamencephalon, 157
 Thalamus, Literature on, 171
 Thebesian valve, 448
 Thompson, J. M., 203
 Thompson, I. MacLaren, 405, 609
 Thompson, P., 24, 589
 Thompson, R., 549
 Thomson, Arthur, 225, 233, 265, 405
 Thoracic duct, 473
 Thorax, Postural modifications of, 566
 —, Shape of, 488
 Thumb. See Pollex.
 Thurnesse, A., 590
 Thymus, 371
 Thyro-glossal duct, 375
 Thyroid, aberrant, 375
 — cartilage, 352, 491
 —, Development of, 374
 —, Origin of lateral lobes, 378
 Tibialis posticus, 624
 Tiegs, O. W., 280, 591
 Tilney, F., 164, 202
 Todd, T. Wingate, 82, 85, 90, 104, 232,
 265, 613, 630, 647
 Todd and Lyon, Closure of sutures, 321
 Todd and Tracey, 232
 Todd and Wharton, 233
 Toenbury, G., 424
 Tomes' fibres, 270
 Tongue, Abnormalities of, 366
 —, Development of, 364
 —, Muscles of, 366
 —, Nerves of, 365
 Tonsil, Development of, 370
 —, Pharyngeal, 368
 Toro, E., 647
 Touch bodies, 664
 Tower, Sarah S., 649
 Trabeculae cranii, 218
 Trachea, 491
 —, Development of, 480
 Transplantation of tissues, 64
 Transposition of parts, 69
 Transverse vertebral processes, 100
 Trapezius, 109, 360, 627
 Traut, H. F., 527
 Tredgold, A. F., 590
 Treitz, Muscle of, 409, 413
 Triangular fibro-cartilage, 634
 — ligament, 575
 Triplets, 67
 Trochanter, third, 644
 Troitzky, W., 233
 Trophoblast, 16, 20
 Trotter, M., 630
 Trotter and Dawson, 665
 Truncus arteriosus, 445, 453
 Tubal pregnancy, 9, 20
 Tuberculum impar, 364
 Turbinate processes, 248, 287
 Turyna, E., 363
 Twins, Identical, 67
 —, Parabiote, 67
 —, Production of, 65
 Twisselmann, F., 62
 Tympanic bulla, 329
 — plate, 259, 325
 — ring, 260
 Tympano-hyal, 351
 Tympanum, 328
 —, Attic of, 329
 Tyson's glands, 548
 Ultimo-branchial body, 375, 376
 Umbilical artery, 466
 — coelum, 409
 — cord, Formation of, 42
 — hernia, 411
 — veins, 385, 438
 — vessels, Evolution of, 38
 Umbilicus, Changing state of, 579
 —, Weeping patch, 411
 Union of parts, 240
 Uotila, U. U., 563
 Upham and Landauer, 665
 Urachal cysts, 544
 Urachus, 544
 Ureter, 410
 Urethra, Formation of, 549
 —, Muscles of, 545
 Urogenital mesentery, 505
 — sinus, 521, 524, 532
 — system, Evolution of, 500
 Urorectal septum, 538
 Uterus, 515, 518
 —, Malformations of, 519
 —, Musculature, of, 519

- Wisdom teeth, 276, 277, 278
 Wisloeki, G. B., 29, 30, 172, 563
 Witchi, E., 75
 Witch milk, 660
 Wood, L., 154
 Woodburne, R. T., 362
 Wood-Jones F., 74, 90, 104, 154, 202,
 203, 263, 326, 341, 367, 377, 393,
 426, 527, 548, 549, 550, 589, 609, 665
 Wood-Jones, F., On premaxilla, 243, 264
 Woodland, W., 563
 Woollard, H. H., 116, 132, 154, 203, 321,
 363, 378, 460, 609, 665
 Woollard and Harpman, 132, 475
 Woollard and Weddell, 610
 Woolf, A. E. M., 293
 Wolff, Dorothy, 342
 Wolff, E., 75, 262
 Wolfian body, 501, 503
 Wolfian body, Fate of, 506
 — bodies, Veins of, 434
 — bulbs, 516, 527
 — duct, 502
 — —, Experiments on, 514
 — —, Induction effects, 515
 — — in male, 508
 — ridge, 504
 Wolff's Law, 646
 Wormian bones, 214, 216, 221
 Wrai, H., 232
 Wrege, M., 526
 Wright, R. D., 649
 Wrisberg, Cartilage of, 492
 Würth, A., 654, 665
 Wustrow, P., 265
 Wyburn, G. M., 48, 104, 590
 Wyeth, F. J., 342
 Wyndham, N. R., 556, 562

